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LUPUS VULGARIS FOLLOWING BCG VACCINATION.

POUL V. MARCUSSEN.

From the Dermatological Department of the Finsen Institute, Copenhagen.

In 1942 K. A. Jensen pointed out that there is a biological probability that certain BCG strains may produce lupus vulgaris in the skin, since the virulence of BCG is only slightly lower than that of tubercle bacilli isolated from lupus tissue (Jensen and Frimodt-Møller, 1936). By inoculation on bile-potato BCG can obtain the same pathogenicity as some of the well-known lupus strains (Jensen, 1949). Further, the infection of the skin and lymph nodes normally produced by BCG is in many cases clinically as well as pathologically indistinguishable from the tuberculous granulation tissue, scrofuloderma, or tuberculosis colliquativa, which often precedes lupus vulgaris—the latter following immediately or after a lapse of many years. A similarity between BCG infection of the skin and the precursor of lupus vulgaris is thus a likely possibility, both from the bacteriological, clinical, and pathological points of view.

Lupus vulgaris is most often diagnosed very late owing to its almost symptom-less course (Tables I and II). Recognition of lupus vulgaris following BCG vaccination must therefore *a priori* be expected to require many years of observation of a great number of vaccinated persons, or be more accidental.

The literature up to 1952 contains only three reports of the development of lupus vulgaris at the site of BCG inoculation. In none of these was BCG originally demonstrated in the lupus tissue.

Lomholt's case, reported in 1944, had at an early stage been described by Kristjansen (1944) as one of lupoid inoculation tuberculosis. T. Jensen (1948) has since revised this case, and Tolderlund (1953), by culture of a biopsy specimen, identified a tubercle bacillus strain that in colony morphology and pathogenicity was indistinguishable from BCG. This was thus the first bacteriologically verified case of lupus vulgaris resulting from BCG vaccination. Kalkoff (1950) and Gilje (1952) have each reported a case in which they did not

TABLE I.—*Interval between Discovery of First Sign of Lupus Vulgaris or Scrofuloderma and Reference to the Finsen Institute for Treatment.*

Number of years.	Number of patients.	%.
0–4	96	33·9
5–9	40	14·2
10–14	47	16·7
15–19	28	9·9
20–24	24	8·6
25–39	25	8·9
40–59	22	7·8
Total	282	100·0

TABLE II.—*Nine Patients with Uncomplicated Lupus Vulgaris on One Extremity Referred to the Finsen Institute for Treatment after* 1940.

No.	Interval between first sign and reference (years).	Age at reference.	Extent of lesion at reference (sq. cm.).	Patient's sex.
1	6	32	85	F.
2	8	16	200	M.
3	20	38	50	M.
4	25	46	4	F.
5	32	32	300	F.
6	40	41	45	F.
7	45	50	600	F.
8	48	48	160	M.
9	48	63	5	F.
Average	30·2	40·7	161	

succeed in finding tubercle bacilli in the tissue. Kalkoff therefore characterized his case as a "*lupusähnliche Reaktion*". The technique for the demonstration of tubercle bacilli in tissue is rather difficult. As the virulence of these bacilli most often is reduced, culture on artificial medium is, as shown by Jensen and Frimodt-Møller (1936), more expedient than inoculation in animals.

In 1952 the Finsen Institute had two cases in which BCG was demonstrated by culture carried out by Dr. Tolderlund in the Tuberculosis Department of the State Serum Institute. In a third case the aetiology was possibly the same, but the pathogenicity of the demonstrated eugonically growing tubercle bacillus strain has not been determined.

CASE REPORTS.

CASE 1.—First seen on 20 February 1952. A domestic servant aged 17, grown up in a non-tuberculous environment. Tuberculosis control at school in January 1950 showed the patient to be tuberculin negative, and she was thereafter BCG vaccinated at a tuberculosis station. After 2 or 3 weeks a papule appeared at the site of inoculation, which later ulcerated. The ulceration healed spontaneously, but the local

reaction continued to spread slowly. As, however, it gave rise to no symptoms the patient found no reason to draw the examiner's attention to it on tuberculosis examination one year later ; at this time the skiagram was normal and Mantoux 10 i.u. was positive with a diameter of 14 mm. After having been vaccinated the patient was employed at two farms with tuberculin-free cattle. She heard nothing of cases of tuberculosis in the neighbourhood, and she gives no history of acute illness before the vaccination.

The skin lesion was discovered accidentally on medical examination 2 years after the vaccination.

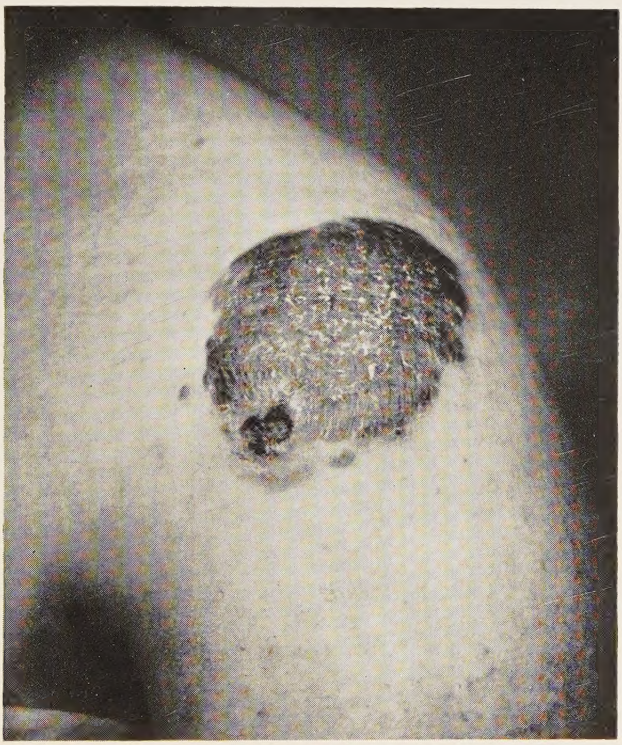

Fig. 1.

On examination.—A lupus plaque about 40 sq. cm. in area on the left deltoid region (Fig. 1). Outside the border scattered lupus nodules. In the centre a small depression corresponding, according to the patient, to the site of vaccination. Two scars due to smallpox vaccination situated one within the border and the other outside the lesion.

Histology (Dr. Fridtjof Bang).—Tuberculoid structure.

Bacteriology.— (*a*) Biopsy 22 February 1952 : After 2 months, scanty growth in two Löwenstein's tubes. Subculture showed moderately pigmented eugonically growing colonies, which on virulence determination (made by intravenous injection into rabbits and intraperitoneal injection into guinea-pigs, with a BCG strain as control) showed that the virulence of the isolated strain paralleled that of BCG. By intracutaneous injection into guinea-pigs no difference was demonstrated between the

isolated strain and BCG. The isolated tubercle bacillus strain and BCG thus proved indistinguishable both as regards colony morphology and pathogenicity in experimental animals (Tolderlund, 1953).

These bacteriological findings were verified by culture from biopsy specimens 9 December 1952 and 12 March 1953.

(*b*) Gastric lavage 22.ii.52, 16.ix.52, 9.xii.52, and 12.iii.53 : no growth of tubercle bacilli.

(*c*) Catheter urine (9 occasions) : no growth of tubercle bacilli.

Skiagrams.—Lungs, 22.ii.52, 19.iii.52, 9.iv.52, 16.ix.52, 9.xii.52, and 12.iii.53 : normal.

Kidneys, 22.ii.52 and 16.ix.52 : normal.

Tuberculin sensitivity : positive reactions 21.ii.52 to 1 : 100,000 ; 9.iv.52 to 1 : 10,000 ; 16.ix.52 to 1 : 1000 ; and 11.iii.53 to 1 : 1000.

General clinical examination normal.

Treatment.—Calciferol (ultranol ultraconc. spir. " IDO "), 480 mg. Dihydrostreptomycin, 20 g. P.A.S., 510 mg.

Result.—Clinically cured by 11 March 1953. Microscopically still shows tuberculoid structure, however, and growth of tubercle bacilli by culture.

Case 2.—First seen on 22 April 1952. A shop-assistant, aged 15, grown up in a non-tuberculous environment. On tuberculosis examination at school the patient was tuberculin negative and was BCG vaccinated three times without obtaining lasting positivity. Before being engaged as a shop assistant in a grocer's she was again, in February 1952, submitted to BCG vaccination at a tuberculosis station. To the patient's recollection she had not been ill before the vaccination. Skiagram showed no abnormality.

Ulceration occurred after the vaccination, which soon healed up, but was followed by a slowly growing plaque. The ulceration was associated with fever, which soon subsided, and with regional adenitis, which persisted and later formed a sinus. One month after the vaccination Mantoux 10 i.u. was positive with a diameter of 12 mm. Skiagram normal.

On examination.—A lupus plaque about 15 sq. cm. in area on the upper part of the left arm with a few nodules outside its border. A hard lymphatic cord, the thickness of a slate pencil, passed from the lower border of the lesion in a distal direction. On the shoulder three scars from previous vaccinations. In the axilla a goose-egg-sized mass of glands with a fistula.

Histology (Dr. Fridtjof Bang).—21.iv.52 and 3.vii.52 : Tuberculoid structure. 20.viii.52 : Cicatricial tissue.

Bacteriology.—(*a*) Biopsy specimen : No growth on culture or inoculation 22.iv.52, 1.v.52, 26.v.52, 20.vi.52, and 3.vii.52.

(*b*) Culture of pus from the fistula revealed a scanty growth of tubercle bacilli, which did not differ from BCG in cultural characteristics and pathogenicity (Dr. K. Rasmussen, Tuberculosis Department, the State Serum Institute).

(*c*) Gastric lavage (4 occasions) : no growth of tubercle bacilli.

(*d*) Catheter urine (4 occasions) : no growth of tubercle bacilli.

Skiagrams.—Lungs, 23.iv.52, 2.vii.52, 20.viii.52, and 11.iii.53 : normal. Kidneys : normal.

Tuberculin sensitivity : positive reaction 22.iv.52 to 1 : 10,000 ; 20.viii.52 to 1 : 10,000 ; and 11.iii.53 to 1 : 100,000.

General clinical examination showed no abnormality.

Treatment.—Isonicotinic acid hydrazide (Diforin " Leo "), 8·4 g. in the course of 55 days.

Result.—Clinically, microscopically, and bacteriologically symptom-free by 20 August 1952. Still under observation.

Case 3.—First seen 12 February 1949. A farm-servant, aged 16. Since 8 years before the patient's birth his mother had been suffering from lupus vulgaris, in which human tubercle bacilli of reduced virulence had been demonstrated. The mother's infection is referable to a patient with pulmonary tuberculosis in a home where she had been employed as domestic servant before her marriage. The family, comprising six members, is tuberculin negative and has been under regular tuberculosis control without other cases of tuberculosis having been found.

The patient was BCG vaccinated at a tuberculosis station on 24 November 1945, about 3 years before attending the Finsen Institute. One year before the vaccination his mother had been under treatment in a sanatorium for lung infiltration, but tubercle bacilli were not demonstrated. At the time of the patient's vaccination his mother had several small lupus lesions on the body, but x-ray of the lungs showed no abnormality. No growth of tubercle bacilli from gastric lavage.

The vaccination reaction grew slowly but caused no other symptoms.

On examination.—A lupus plaque about 100 sq. cm. in area on the left deltoid region. Scattered lupomas outside the lesion. Site of vaccination cicatricial.

Histology (Dr. Harald Gormsen).—Tuberculoid structure.

Bacteriology.—(*a*) Biopsy 18.ii.49 : Growth of tubercle bacilli of the eugonic type. Their virulence was not determined and it is impossible to decide whether they were a BCG strain.

(*b*) Gastric lavage 4.ii.53 : No growth of tubercle bacilli.

(*c*) Catheter urine 4.ii.53 : No growth of tubercle bacilli.

Skiagrams.—Lungs, 17.ii.49, 6.iv.49, 25.iii.50, 5.i.51, 13.ii.52, and 4.ii.53 : small calcified area in the right hilum, unchanged from 1949 to 1953. Kidneys, 17.ii.49 and 5.i.51 : Normal.

Tuberculin sensitivity : positive reaction 21.ii.49 to 1 : 10,000 ; 24.iii.50 to 1 : 1000 ; and 4.ii.53 to 1 : 10,000.

General clinical examination normal.

Treatment.—Calciferol (ultranol ultraconc. oleosum " IDO "), 983 mg.

Result.—Clinically and microscopically symptom-free after 7 months of treatment. No recurrence after 4 years of observation.

According to the data obtained there is a theoretical possibility that the patient may have been infected by his mother at the site of vaccination with BCG. This must, however, be regarded as rather unlikely, as the mother had only small lupus lesions on the body and had had her lungs x-rayed and her gastric lavage secretion examined with negative results. The patient lived at home for one month only, otherwise staying as a farm-servant at farms with tuberculin-free cattle and with no known case of tuberculosis among the staffs.

Discussion.

The clinical and microscopical picture of these three cases is pathognomonic of lupus vulgaris, and the slow destructive growth is typical. There is much evidence to suggest that the three cases were due to the vaccination, since the lesion arose from the site of vaccination and developed as a continuation of the reaction. The demonstration of BCG by culture from the tissue in Case 1 and in pus from a fistula in the drainage area in Case 2 must be taken as a proof that these cases, like that reported by Lomholt, were caused by BCG. Further, tuberculosis was not present in the environment, either before or after the vaccination, and no signs of other tuberculous infection could be found by thorough examination of the patients. In Case 3 bacteriological proof is lacking owing

to inadequate examination, and there was found a case of lupus vulgaris in the family.

In Cases 1 and 2 the lesion occurred in perfectly healthy persons living in non-tuberculous environments and, as far as could be ascertained, with no acute illness or debility prior to the vaccination ; in this they differ from the case of Engelbreth-Holm and Eskelund (1952) in which abscesses occurred after BCG vaccination. The vaccination had been carried out in circumstances which are common in this country, the usual precautionary measures had been taken, and the immediate reaction had not been unusual.

The three cases described above raise the total number of reported cases of lupus vulgaris following BCG vaccination to six. Of these, three were certainly due to the vaccination and three probably so.

On the basis of present knowledge concerning the pathogenesis of lupus vulgaris these cases are not surprising. They are to be regarded as a probably rare manifestation of the BCG infection. Lupus vulgaris produced by human or bovine tubercle bacilli is in 30% of cases preceded by a tuberculous granulation tissue, scrofuloderma or tuberculosis colliquativa. Further, according to Moncorps (1941, 1947), every 12th or 13th child in whom colliquative tuberculosis has been diagnosed will develop lupus vulgaris, though as a rule after an interval of 3 or 4 years ; often they are not treated until many years later. BCG always produces granulation tissue at the site of inoculation or in regional glands, and this in some cases is so extensive that it clinically corresponds to colliquative tuberculosis (Kalkoff, 1951 ; Catel and Daelen, 1950 ; Bruns, 1949 ; Borecka and Wojtkiewiczowa, 1951), so that one of the conditions for the development of lupus vulgaris is present. The mode of transition from colliquative tuberculosis to lupus vulgaris is unknown, but a reduced virulence of the tubercle bacilli in the skin together with the development of strong tuberculin allergy are supposed to play a decisive part. Griffith (1932), Andersen (1921), Jensen and Frimodt-Møller (1936), and Tolderlund (1946) have found bacilli with reduced virulence in 50 to 86·8% of examined cases of lupus vulgaris. The virulence has often been found to correspond almost to that of BCG (Jensen and Frimodt-Møller, 1936). Further, it may be observed that Jensen (1949) takes such low-virulence, slowly multiplying types of bacilli with a pronounced power of producing granulation tissue (resting forms) to be of great importance in the pathology of tuberculosis.

It is impossible to say whether the variations demonstrated by Tolderlund (1952) in the concentration of viable bacilli in BCG vaccine due to the influence of light played any part in the pathogenesis of the observed lupus cases. Case 1 occurred after treatment with winter vaccine, which has been found to contain a relatively large number of living germs. Case 2 likewise occurred after treatment with winter vaccine, but at a time when the damaging influence of light was controlled. According to Bøe (1950) there are, however, considerable

seasonal variations in the incidence of other complications of BCG vaccination if the content of viable germs in the vaccine has not been controlled.

The few observed cases of lupus vulgaris after BCG vaccination are of no importance for an evaluation of the vaccination as such. They prove, however, that BCG may give rise to very protracted infection in man.

The fact that four of the six cases observed have occurred in Denmark, where both BCG vaccination and the question of lupus have for long been subjects of particular study, as well as the experience that lupus develops very slowly and without symptoms, indicate the need for follow-up, at least in the cases where granulation tissue persists after the vaccination. This period of observation should probably take place even if the granulation tissue resolves, since in lupus vulgaris there are often found microscopic foci more than a centimetre outside the visible lesion, and in colliquative tuberculosis retrograde lymphangitis often extends a considerable distance. According to experience with lupus vulgaris, this control ought to extend over not less than 5 years after the vaccination. Further, attention should no doubt be given to the possible occurrence of the rarer forms of tuberculosis of the skin and of tuberculides, which are not well known outside dermatological clinics and departments.

Such a follow-up should be practicable, as the number of strong reactions seems to be relatively small (øster, 1950 ; Hertzberg, 1948).

Cases of lupus vulgaris following BCG vaccination ought probably to be treated in the same way as ordinary lupus and as early as possible, because the deltoid region is known by experience to be an area where cosmetically satisfactory results are difficult to obtain.

Summary.

1. Three cases of lupus vulgaris are described, of which two were certainly caused by BCG vaccine. A total of six such cases have now been reported, of which three were certainly and three very probably due to BCG.

2. The cases are supposed to represent a rare form of manifestation of infection with BCG, and not an accidental complication.

3. The occurrence of these cases does not influence the evaluation of BCG vaccination in general.

4. It is recommended that cases where persisting granulation tissue has developed after vaccination should be kept under observation for a period of not less than 5 years, even though the granulation tissue resolves.

5. Treatment should be the same as for ordinary lupus vulgaris ; it should be started as early as possible owing to the poor cosmetic results often obtained on the deltoid region.

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IDIOPATHIC ENLARGEMENTS OF THE LIPS: CHEILITIS GRANULOMATOSA, ASCHER'S SYNDROME AND DOUBLE LIP.

G. H. FINDLAY,

Department of Internal Medicine, University of Pretoria.

Lip enlargements make a chaotic class. Conditions as diverse as the hereditary Hapsburg lip, accidental vaccination on the lip and the thick lips of cretinism must be included in an adequate classification. Furthermore, some lip swellings may be encountered in which the underlying process is obscure. Five cases of this kind are presented here.

Cheilitis Granulomatosa.

Essential granulomatous cheilitis or cheilitis granulomatosa, as described by Miescher in 1945, is a condition in which the buccal surfaces of the lips enlarge and are infiltrated typically with " sarcoid " tissue. The tongue and cheeks may be similarly involved (Schuermann, 1952). Some twenty years before Miescher's account appeared, Melkersson had described a recurrent facial palsy, sometimes bilateral, associated with chronic lip enlargements. Rosenthal had also discovered a lingua plicata in these cases (Jordan and Reichel, 1950). Then, in 1950, the Melkersson-Rosenthal triad of relapsing facial palsy, thick lips and lingua plicata was found by Richter and Johne to show the same " sarcoid " histological structure in the affected lips as Miescher's cases of cheilitis granulomatosa. Since then, many have agreed that the same condition had been independently described. The disease often starts with an abrupt oedematous swelling of the lips, often of the lower lip alone. It persists for several weeks with periods thereafter of incomplete regression and relapse. The histological picture suggests Boeck's sarcoid, but sarcoidosis and other known causes of chronic granulomata of tuberculoid structure are evidently not responsible for the changes. Further information and reflection on these topics may be found in articles by Miescher and Storck (1951), Gahlen and Bruckner (1951) and Tappeiner (1953).

Case 1.—A 19-year-old Bantu man complained of enlargement of the lower lip for two years. The swelling had appeared overnight and there had been no previous lesion or injury of the lip. No drugs had been taken. The family history was not relevant.

The lower lip was found to be everted with swelling of the buccal surface, slight scaling and some midline fissuring (Fig. 1). The lip felt slightly nodular and elastic. A small quantity of clear secretion could be expressed through the buccal gland

openings. A well circumscribed hypertrophy was also present along the inner sides of the cheeks in their lower anterior parts, giving a fulness to each cheek behind the depressor anguli oris muscle. The resulting heaviness of the lower part of the face suggested a facial palsy, which was in fact not present. The tip of the tongue also was infiltrated, and the folds of a lingua plicata were obvious.

Wedge resection of the lip was performed. The tissue thus removed showed that three inflammatory abnormalities were responsible for the lip enlargement : a peri-capillary cell emigration, a nodular sarcoid type of cell proliferation and a diffuse oedema with an increase of fibroblasts.

The densest pericapillary cell masses were seen in the papillary layer of the corium and in between the acini of the labial salivary glands. Lymphocytes, mast cells, plasma cells, fibroblasts and oedema were evident.

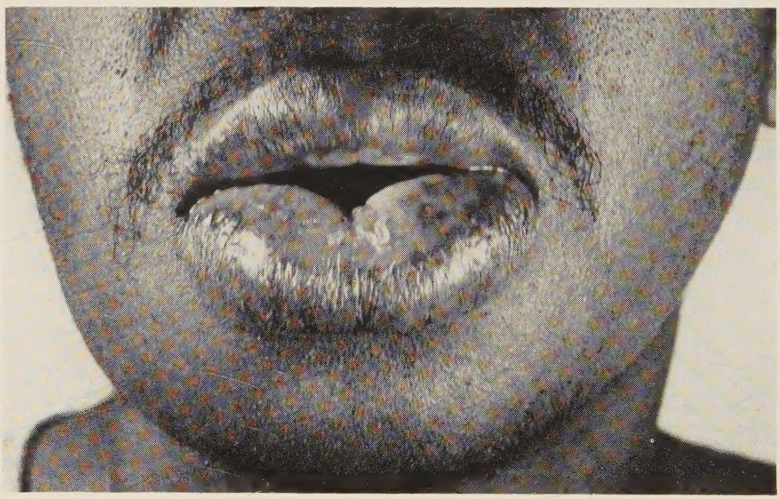

FIG. 1.—Case 1. Cheilitis granulomatosa.

The " sarcoid " nodules stood chiefly near capillaries and venules, usually at the sites of vascular confluence or small neurovascular bundles. Blood vessels were present only at their edges. These nodules showed signs of internal tension : surrounding collagen was compressed, venules were indented and stretched across the periphery, the proliferating reticular cells in the nodules were watery and a tense intercellular oedema was observed. Vessels on the outside of these masses showed lymphocytic emigration along their concave sides as they curved round them. Coronal sections of the lip displayed this nodular arrangement more clearly than sagittal sections. The cellular composition of these nodules was fundamentally that of a proliferating and differentiating reticular-cell syncytium, which produced mainly lymphocytes amid a number of aberrant and necrotic cells and fibrils. Fibroblasts were formed as well as giant cells of Langhans type which arose apparently by amitotic division of reticular or fibroblast cell types. In areas where the intercellular oedema was less tense, monocytes tended to form. These cell relationships were deduced by observing protoplasmic continuity and continuity along the framework of reticulum, and also by tracing transitions between cell types.

The last type of reaction which contributed to the size of the lip was an increase in fibroblasts, capillaries and oedema in the tissue deep to the granulomas.

The vascular channels throughout were wide. The arteries, arterioles and subpapillary venous plexus were little involved in the inflammation. Where identifiable, the lymphatics were normal. Likewise, the labial salivary glands and their ducts revealed no intrinsic abnormality. A few features of the epidermis were noteworthy. The rete pegs showed marked slender prolongations, though the stratum spinosum remained thin. The epithelium showed little oedema ; slight spongiosis of the basal layer and some watery cells just below the parakeratotic stratum corneum were seen. In a few places there were pyococcal pustules in the stratum corneum which were plainly the prelude to the formation of the central fissure in the lip. The only other important feature was the presence of a number of the epidermal colloid bodies of Civatte. They were situated in the stratum corneum above the rete pegs, apparently in process of exfoliation.

Ascher's Syndrome.

Ascher's syndrome is another condition in which swelling of the lips is found. It occurs together with an analogous relapsing oedema of the upper eyelids, producing blepharochalasis. The lips are said to be enlarged by the presence of hyperplastic labial salivary glands, but these glands by themselves could hardly give rise to the recurrent increases in swelling which are a feature of the syndrome. A mass of yellow tissue may be removed at operation from beneath the relaxed skin of the eyelids. This mass sometimes consists of prolapsed orbital fat, but it has also been found to be formed largely of lacrimal gland tissue. In the original account of the syndrome by Ascher, a further element was mentioned—a non-toxic goitre. Evidence was also advanced in favour of a hereditary origin. The papers by Ascher (1920) and Wirths (1920) are noteworthy. Futher reports have also appeared by Ascher (1922), Eigel (1925), Rosenstein (1932), Hartmann (1932) and Eisenstadt (1949).

Case 2.—A 17-year-old Bantu man complained of general swelling of the lips and drooping of the upper eyelids for 6 months. Over periods of a few weeks at a time the swellings showed exacerbation and remission. Nothing further of significance was discovered in the history.

There was a gross ectropion of both lips due to swelling of the mucosal portion (Fig. 2). Inside the mouth the baggy thickening of the lip musosa disappeared gradually into the tissue of the cheeks. Mucosal thickening was also seen on the forepart of the hard palate, in the nose and in the palpebral conjunctiva. No goitre, facial paresis, lingua plicata or other abnormality was found. His skin, however, was of a remarkably silky texture. The redundant tissue was resected from the lips and upper eyelids.

The upper eyelids each contained a mass of yellow tissue behind the orbicularis oculi. This was taken to be prolapsed orbital fat, but histological examination showed that it consisted of lacrimal gland substance throughout. From its position across the eyelid, it could only have been formed by a hyperplasia of the accessory lacrimal glands of Krause. Within the lobules formed by the hyperplastic acini there were scattered lymphatic germinal centres. Plasma cells were present between the acini. Blood and lymph channels were dilated. Between the gland lobules a loose areolar tissue was present with some fat cells as well.

The upper lip (Fig. 3) showed two main causes for enlargement : cellular infiltration with oedema in the periglandular connective tissue and great dilatation of what

appeared to be the gland ducts. The remaining connective tissue was more vascular and cellular than usual, but presented little qualitative abnormality. The inter- and peri-glandular connective tissue showed areas of vascular and oedematous reticular-cell proliferation with stretching and compression of the gland masses. The reticular-cell differentiation was chiefly towards the formation of numerous plasma cells. There were intermediate cell types, multinuclear forms (but no Langhans giant cells), necrobiotic changes and diverse types of Russell bodies.

FIG. 2.—Case 2. Ascher's syndrome.

Fibroblasts were also formed, with some histiocytes and a few lymphocytes as well. Around some of the ducts there were deposits of mucin in the connective tissue.

The duct system was greatly dilated. In one duct followed in serial section to the surface, the outlet was patent. The only conceivable cause for an obstruction was a parakeratotic epithelial cushion at the outlet itself. Some of the ducts showed a semiglandular structure. Here the duct cuticle was absent and the cells often multilayered, with a variable and even gross vacuolation of the surface cells. Some of these cells apparently secreted mucus, being pyroninophilic, sometimes of goblet shape and having secretory vacuoles that were positive to periodic acid-Schiff with a γ-metachromasia. Otherwise, the duct dilatation led to stretching and flattening of a fairly normal duct wall. The secretions in the ducts were nowhere specially dense or abundant. The cell infiltrates were not specifically perivascular. Most of

the vessels were normal, except that the venules showed some great cavernous dilatations near the dilated ducts, and the capillaries and venules tended to show endothelial swelling and vacuolation. A few lymphatics were seen and considered to be normal. The epithelial changes are discussed under a separate heading.

The lower lip was less swollen than the upper, and the histological changes differed in degree but not in type. The greatest bulk of the portion of the lip removed consisted of vascular connective tissue, and large venous spaces were again seen.

FIG. 3.—Case 2. Ascher's syndrome. Section of upper lip showing periglandular granulomas and dilatation of the ducts. Hale's dialysed iron technique, mucin dark.

The glands showed the same types of inflammatory change between the acini, but they were certainly not increased in size or number, and the duct systems were less dilated than in the upper lip.

CASE 3.—A 24-year-old Bantu woman complained of a swollen upper lip which had developed gradually at the age of 7. When she was 14 a plastic operation on the lip had been attempted elsewhere. Only a partial reduction in size had resulted and the swelling had not since increased. Also in her seventh year she had had an episode of gross swelling of the eyelids with severe headache, lasting about a week. Ever since then her upper eyelids had drooped slightly. The swelling of the eyelids had never recurred. Apart from the abnormal shape of the lip, she complained of excessive lacrimation on reading and a constant salivary discharge from the duct

openings on the lip She also suffered from frequent headaches. A severe mitral stenosis was present, and this was successfully treated later by valvotomy.

Examination showed a loose, lobulated upper lip fold lying behind the normal closure line of the lip. Glands were palpable in the fold and a clear secretion could be expressed. The epithelium was intact and there was an old surgical scar on the deep surface. A mild blepharochalasis of the upper eyelids was evident, and in the outer part of one of the lids a small nodule could be felt. The thyroid was just palpable. The lower lip, cheeks, tongue, palate, nose and the remainder of the integument were normal.

Wedge resection of the redundant part of the upper lip was performed. Histological examination revealed changes essentially similar to those in the upper lip of Case 2. There was, however, a general increase of dense fibrous tissue in the submucous and inter- and periglandular areas. The mixed gland acini and gland ducts were also variably stretched and widened. One of the ducts showed a number of secretory mucous cells along its course. The composition of the interacinar tissue differed. There was a vascular, fibrous and cellular increase in which collagen fibres predominated. There were a few inconspicuous foci of oedematous reticular-cell proliferation. The cells present were chiefly mast cells, fibroblasts and mature plasma cells, the last containing some Russell bodies. A few lymphocytes also were seen.

Case 4.—A 42-year-old European man was found to show an obvious nodular thickening of the mucosa of both lips with loose overlying tissue. He also had heavy upper eyelids. The condition of the lips had developed slowly from the age of 17 without any abrupt episodes of swelling or subsidence. The mild blepharochalasis had been observed later. He further showed a polycythaemia resulting evidently from emphysema, and a small stature with retarded genital development. His intellectual and emotional growth also seemed handicapped, despite an alert mental attitude.

A biopsy was permitted on one of the prominent masses inside the lower lip. The greatest bulk of the specimen was composed of seromucous gland acini with little increase of connective tissue between the gland lobules (Fig. 4). Cell infiltration was sparse and was confined to small quantities in the connective tissue and between the acini. The periacinar or pericapillary reticular cells tended to differentiate towards plasma cells with the production of many imperfect and degenerate forms, and to a less extent towards histiocytes and fibroblasts. There was some dilatation of the veins. The glands themselves and their ducts, the blood and lymph vessels and the connective tissue elsewhere in the specimen were otherwise normal. The epithelial changes are discussed separately.

Double Lip.

Double lip is an abnormality best seen in the upper lip. The lip can be divided anatomically into external vermilion and internal buccal portions which meet at the normal line of closure of the mouth. If the buccal portion swells, a furrow appears at the closure line. This furrow makes the enlarged buccal part project as an extra fold inside the external vermilion, and in this way a double lip is produced. It is made obvious when the lips are tensed during speaking and smiling. Double lip is one of the features of Ascher's syndrome, but when it occurs as an isolated anomaly it is usually present from early childhood and recurrent increase in the swelling does not occur. The inner fold consists usually of lax mucosa overlying prominent labial salivary

glands. Mild degrees of double lip formation are not rare and may be associated with slight blepharochalasis. This suggests that no sharp line can be drawn between cases of congenital double lip and the gross varieties of Ascher's syndrome. The subject has been discussed by Conway (1938) and Calnan (1952).

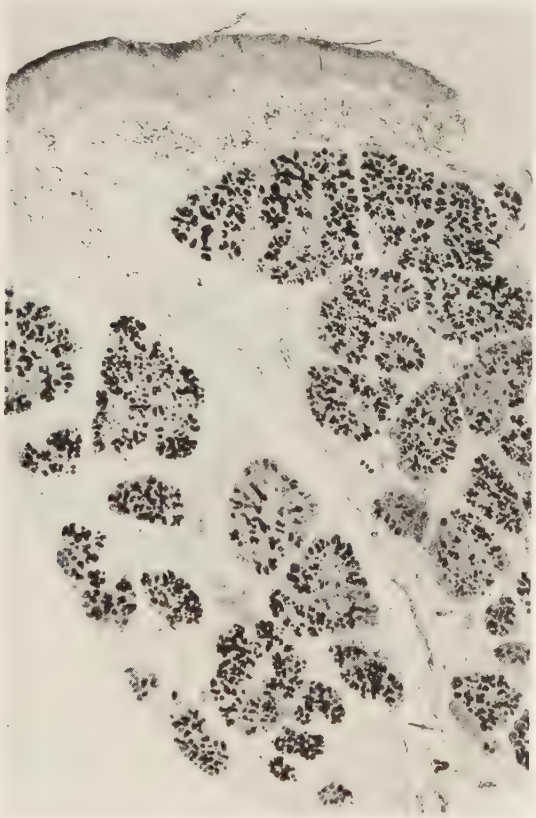

Fig. 4.—Case 4. Ascher's syndrome. Section of lower lip showing hyperplastic salivary gland mass. Gomori's hexamine-silver nitrate method, mucin black.

Case 5.—A 20-year-old Bantu man showed a distinct double upper lip which had been present as long as he could remember. There was also a soft thickening of the inner aspect of the lower lip and lower anterior portions of the cheeks. There was no history of recurrent swelling of these tissues. The palate and alveolar margins appeared to be abnormal in shape, the palate being high, narrow and sharply arched, and the maxillary tooth rows very nearly parallel to each other with broad and flat alveolar margins. No other abnormalities were noted. The upper double lip was resected and a biopsy was also taken from the lower lip.

The upper lip consisted largely of loose vascular connective tissue. The seromucous glands were normal in structure and size; between them and around the vessels there was a little infiltration of lymphocytes, plasma cells and mast cells.

The gland ducts also were normal, though they contained an occasional flat fibrillar and pyknotic cell. No other abnormal features were observed.

The lower lip biopsy was taken from one of the prominent mucosal masses. The specimen resembled that from Case 4: The mass consisted of large seromucous gland lobules with some surrounding loose connective tissue.

Histology of the epithelia (*Cases* 2–5).—A combined description of some special features will be given.

Passing from the lip epidermis to the buccal mucosa, the stratum granulosum in the epidermis was seen to sweep down and disappear in a position just a few cells above the basal layer in the mucosa (Fig. 5). This indicated that the prickle cells, which in the epidermis lay below the stratum granulosum, occupied a morphologically supra-granular position in the mucosa. These differences between epidermal and

FIG. 5.—Case 2. Transition from epidermal to mucosal type of cornification in the lip. Stratum granulosum sweeps down towards the basal layer in the mucosa.

mucosal prickle cells were brought out further by the following observations. The *epidermal* basal and prickle cell layers together formed a more or less uniform layer of non-vacuolated basophilic and pyroninophilic cells. In the *mucosa* these features were confined to the lowermost epithelial cells only. In contrast the mucosal prickle cells were also paler and larger. They were pleomorphic and had lost their basophilia. They appeared more watery, showing a variety of prominent intranuclear vacuoles and cytoplasmic vacuoles of a large central or diffuse honeycomb type. Vagueness and even loss of the nuclear membranes was noted. A basket-weave pattern was produced by the peripherally condensed cytoplasm of adjacent prickle cells with large central vacuoles. The cytoplasm of these cells was apt to take the methyl green, periodic acid-Schiff (PAS) and Gram stains. In the upper layers some of the PAS-positive material appeared to be displaced into the intercellular spaces. This material was not glycogen, being resistant to the action of ptyalin and failing to stain with Best's carmine.

The labial gland mucin (*Cases* 2, 4 *and* 5).—The intracellular labial gland mucin was investigated histochemically. It was found throughout to be a true mucin (acid mucopolysaccharide), possibly not very highly polymerized, and without any evidence of a protein conjugated to it in the molecule. This differs from the observa-

tion of Lennox, Pearse and Richards (1952), who found that normal buccal gland mucin was a heavy complex molecule containing acid mucopolysaccharide and protein.

Technical summary of mucin tests.—Formalin-fixed paraffin sections were used, except for Carnoy fixation in Case 3. The intracellular mucin reacted as follows: Best's carmine, negative; Southgate's mucicarmine, positive; PAS, + +; ptyalin digestion and PAS, ++; Hale, positive. Metachromasia, +, β-type at pH 7, and virtually negative at pH 3·8. Methylene blue extinction: incomplete extinction at pH 3·88 in all specimens. Protein tests: Millon, coupled tetrazonium and Gram reactions, negative.

Methylene blue extinction (Pearse, 1953) showed much uneven and partial binding of the methylene blue. Some acid solutions showed less "extinction" than more alkaline ones. Relative staining intensities could often be established without looking at the mucin, by holding the slides to the light. The value of the test was therefore questionable. In the *coupled tetrazonium reaction* an easy way of tetrazotizing benzidine was found to be that of Täuber (1894). Saunders (1949) moreover recommends a temperature of 10–14° C. for tetrazotization. Pearse's (1953) formula for tetrazotizing benzidine probably contains too little nitrite, and various side reactions can be expected.

Comment.

It is obvious that while Ascher's syndrome and double lip may be related to each other, cheilitis granulomatosa is related to neither. Professor Miescher, who kindly examined sections from Case 2 of Ascher's syndrome, agreed that they do not resemble the changes of cheilitis granulomatosa. Clinically, the the lips in Ascher's syndrome and cheilitis granulomatosa may nevertheless be hard to distinguish. In Ascher's syndrome, however, the upper lip is most often involved and in cheilitis granulomatosa the lower. The swellings in Ascher's syndrome also tend to be more lobulated, discrete and soft while in cheilitis granulomatosa they are more diffuse, tense and elastic. Otherwise the clinical differentiation must be made on the associated features.

The colloid epidermal bodies of Civatte were noted in the case of cheilitis granulomatosa reported. They are usually, though not exclusively, associated with drug eruptions (Civatte, 1950). Some endogenous chemical allergen may therefore be important in the pathogenesis. The recurrent swellings and facial palsy may be due to acute reactions in the granulomas which are situated along neurovascular bundles, but the most distinct granulomas seem to be too near the epithelium to do much damage in this way.

In Ascher's syndrome and double lip a connective tissue increase is important in producing lip enlargement. On the other hand, in two of the specimens of the present series, it was obvious that the labial salivary gland mass can be almost entirely responsible for the enlargement, and the same applies to the excess of lacrimal tissue in the eyelids. Nevertheless, a fibrocystic and inflammatory change of the labial salivary glands is also prominent. These changes may resemble those of the infantile mucoses, as in fibrocystic disease of the pancreas. However, the pathological and histochemical studies

described here did not suggest that a particularly viscid mucin was responsible for the gland changes. It is possible though that the lips may swell suddenly after spontaneous rupture of one of the dilated ducts.

The present cases were all treated by wedge resection of all the diseased tissue. A broad strip of epithelium must be taken away to obtain a good cosmetic result, and it is probably important to see that all the underlying gland tissue is removed. The immediate result was excellent in all the cases.

Summary.

Five cases of chronic enlargements of the lips are presented. One was an example of cheilitis granulomatosa with an inflammatory infiltrate of sarcoid type in the lips, and infiltration of the tongue and cheeks. A lingua plicata was present. The trend of reticulum-cell differentiation was studied, the relation of the infiltrate to neurovascular bundles was noted, and the epidermal colloid bodies of Civatte were found suggesting the presence of an endogenous chemical allergen.

In three cases the diagnosis of Ascher's syndrome was suggested on the presence of an acquired double lip with blepharochalasis. One case of congenital double lip was also described which did not differ essentially from the Ascher cases. The mildest examples showed a connective tissue increase in the lips. More advanced cases showed a reticulofibrocystic change in the glands of the lips with a variable degree of glandular hyperplasia, and secretory metaplasia of the gland ducts. In one of the cases the accessory lacrimal glands were also hyperplastic. The mucus secreted by the labial salivary glands in these conditions was thinner and less complex than normal.

A study of the transition from skin to mucosa across the lip in these conditions led to the conclusion that the stratum spinosum of the epidermis was not homologous with the stratum spinosum of the mucosa.

The writer wishes to thank Dr. Albert Myburgh of the Department of Surgery, Pretoria University, for the surgical treatment of all the cases.

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EPIDERMOLYSIS BULLOSA RESEMBLING JUVENILE DERMATITIS HERPETIFORMIS.*

G. B. DOWLING, M.D., F.R.C.P.,
Director, Institute of Dermatology, British Post-Graduate Medical Federation, University of London;

AND

R. H. MEARA, M.B., M.R.C.P.,
Registrar, St. John's Hospital for Diseases of the Skin.

We wish to describe a small group of children suffering from a bullous eruption, which, although morphologically resembling juvenile dermatitis herpetiformis, is without doubt either epidermolysis bullosa or very closely related to it. There are, however, certain features common to all four cases which are unlike epidermolysis bullosa and which make it difficult to fit them into the generally accepted classification of this group of diseases.

These cases are being described because they seem to constitute a separate clinical entity the precise nosological position of which is open to argument. Certainly all four cases are strikingly similar in their clinical appearance. There can be no doubt that similar cases have been labelled juvenile dermatitis herpetiformis and there is a remarkable resemblance between the lesions of senile dermatitis herpetiformis, or bullous pemphigoid, and those occurring in the cases under discussion.

Clinical Description.

There are four children to be described suffering from this condition, three girls and one boy. Their ages range from 3 to $7\frac{1}{2}$. In three cases the condition was present at birth or appeared within 72 hours of birth, and in the fourth case it started at the age of three months. During infancy the disorder increased in severity and since then has remained more or less the same except in the oldest child, a girl aged $7\frac{1}{2}$, in whom there has been considerable improvement during the past year. There is a clear relation between the development of some of the bullae and trauma although many lesions appear to arise spontaneously.

There is no evidence of a similar condition in the families of any of the patients including 13 living siblings. Blisters occur on any part of the body but are most frequent on the palms and soles (Fig. 2 and 3), around the mouth and on

* Paper presented at the 33rd Annual Meeting of the British Association of Dermatology on 27 June 1953.

the trunk (Fig. 1). In one child there are frequent blisters on the mucosa of the mouth and tongue. Bullae may arise on normal skin or may be preceded by erythema and quite often are haemorrhagic. Papules and urticarial lesions are not seen. The blisters may heal within a few days or may spread peripherally, healing at the centre so that circinate patterns of bullae may develop

Fig. 1.—To show circinate outline of some of the lesions.

(Fig. 1). On healing they leave no trace other than some faint staining which gradually fades.

In the three older patients the palms and soles show irregular hyperkeratosis but the youngest does not, as yet, show this change. This hyperkeratosis is getting much less obvious in the oldest patient who, as already mentioned, appears to be slowly recovering from the disorder. The nails are unaffected except for one or two which show dystrophy where they have been directly involved in blister formation. The teeth of two of the children are carious

FIG. 2.—Hyperkeratosis and blisters of palms.

FIG. 3.—Hyperkeratosis and blisters of soles

although not grossly malformed. There is no evidence of any scarring or atrophy following the bullae and no epidermal cysts are present in any of the children. A biopsy was performed on the oldest patient, a recent blister, less than 24 hours old, being excised. The section shows a subepidermal bulla (Fig. 4).

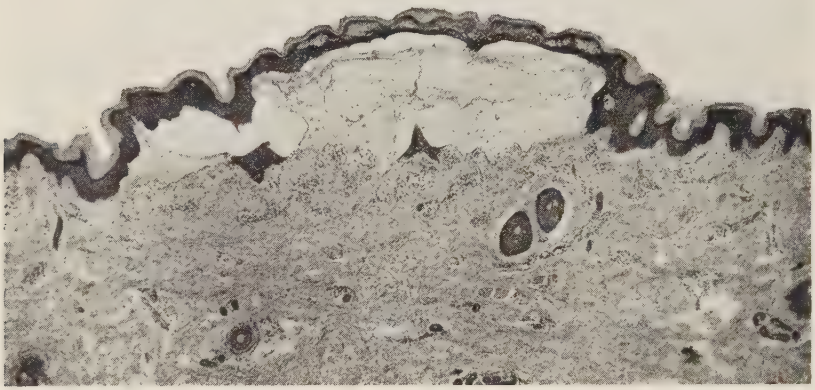

Fig. 4.—Sub epidermal bulla. × 103.

Comment.

These cases clinically resemble juvenile dermatitis herpetiformis as has been indicated by the title of this paper. In fact, cases similar to these now described have been considered to be a juvenile variant of dermatitis herpetiformis. It is generally accepted that dermatitis herpetiformis in infants is very uncommon. Those cases that have been described often appear to bear a more close resemblance to senile dermatitis herpetiformis than to ordinary dermatitis herpetiformis of adults. Søbye (1946) described four cases of dermatitis herpetiformis in infants, the ages of onset being between 4 months and 9 months. Morphologically the lesions resembled those of the cases now described but did not involve the palms or soles and trauma did not appear to be a factor in their production. Herpetiform dermatitis in Søbye's young patients appeared to occur in attacks with periods of freedom intervening. Berlin (1952) described a group of ten children with dermatitis herpetiformis. Here again the appearance of lesions with serpiginous and circinate outlines is mentioned. The palms and soles of these children, however, were always free from blisters.

The resemblance of our cases to juvenile dermatitis herpetiformis is almost certainly fortuitous. The history and other features of the condition from which these children are suffering show that it is most likely to be a congenital defect of the skin which, if genetically determined, must be due to a recessive

factor. The development of blisters following trauma particularly on the palms and soles and the onset of the condition in the first weeks of life strongly suggest that these cases are related to congenital epidermolysis bullosa. However, they do not fit into the classification of this disorder suggested by Touraine (1942) as, although recessive, they are not truly dystrophic. Scarring, milia formation and loss of nails have not been observed. There are nevertheless certain features present which are commoner in the dystrophic recessive type of epidermolysis bullosa. These are the early onset of the condition, the presence of mucous membrane lesions in one child, and the spontaneous development of some of the bullae. Central healing of lesions with peripheral spread producing a circinate outline to many of the lesions has not been described, to our knowledge, in epidermolysis bullosa. It is this clinical appearance in particular which produces the resemblance to juvenile dermatitis herpetiformis and which is one of the features which make it difficult to determine the place of this condition within the congenital epidermolysis bullosa group.

Acknowledgments are due to the Department of Medical Photography, Institute of Dermatology, for kindly providing the photographs.

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THE ABSORPTION OF GRENZ RAYS AND LOW VOLTAGE X-RAYS BY LOCAL APPLICATIONS.

D. S. ANDERSON, M.D., M.R.C.P., D.M.R.T.,

First Assistant, Radiotherapy Department, St. John's Hospital for Diseases of the Skin ;

H. S. WILLIAMS, B.Sc.,

Principal Physicist, The Royal Free Hospital,

and

A. V. STOCKLEY, M.A.,

Assistant Physicist, The Royal Free Hospital.

It was decided recently that it would be interesting to investigate the effect of the presence of local applications on the skin during Grenz ray and x-ray therapy. Most of the local applications contained one or more metallic substances which would screen the radiation, so that a variable proportion of the primary beam would be absorbed by the skin. The non-metallic components of these applications were not considered to be important screening agents.

Method.

Grenz rays.—Ten commonly used medicaments were chosen for investigation ; the details of their metallic composition are given in Table I. A sheet of lead foil 0·22 mm. thick was taken and ten holes 1 cm. in diameter were punched out in it. One side of the lead foil was backed with Sellotape.*

Readings were taken of Grenz ray transmissions, first through the Sellotape alone and then through the local applications, which were introduced into the ten holes and smoothed off to the surface so that they were 0·22 mm. in thickness. All readings were made with a Siemens dosage rate meter with a special Grenz ray chamber.

The Grenz ray apparatus was used with the following physical factors : (i) 9 kV 20 ma. 10 cm. focal skin distance. (ii) 12 kV 20 ma. 10 cm. focal skin distance.

X-rays.—A second sheet of lead foil 0·22 mm. thick was taken and prepared as described above, with the exception that the holes for the ointments had a greater diameter and were oblong shaped so that readings could be taken with a Victoreen dose meter.

* Cellulose pressure-sensitive tape.

The x-ray apparatus (designated K.X. 10) was used with the following physical factors : 90 kV 6 ma. Half value layer 1·40 mm. aluminium ; focal skin distance 22·5 cm.

Results

In the case of the Grenz rays the absorption is entirely by the photoelectric effect, and with x-rays generated at 90 kV absorption is mainly by this mechanism. Therefore, the absorption increases rapidly with increasing atomic number, and the presence of metals of comparatively high atomic number in the applications used in dermatology suggested that the absorption or screening by even thin layers of these applications might be appreciable.

From Table I it can be seen that the amount of absorption of the ionizing radiations by the various local applications varies in general with their metallic

Table I.

Local application	Metallic composition.	Percentage transmission. Grenz rays. 9 kV.	Grenz rays. 12 kV.	X-rays 90 kV.
Titanium dioxide paste	20% w/w titanium dioxide ; 25% zinc oxide ; 10% kaolin (hydrated aluminium silicate) ; 2% ferric oxide.	6·25	9·72	64·0
Zinc cream	32% w/w zinc oxide.	18·6	22·2	76·5
Yellow mercuric oxide paste	1% w/w mercuric oxide ; 25% w/w zinc oxide	23·4	35·2	84·0
Calamine compound ointment	12·5% w/w calamine ; 12·5% w/w zinc oxide	25·9	36·7	83·0
Zinc paste	25% w/w zinc oxide.	33·9	44·2	85·0
Calamine cream	7% w/w calamine ; 7% zinc oxide	47·5	61·6	90·0
Glycerine of lead ointment	16·7% glycerine of lead	58·4	66·9	95·0
Titanium dioxide cream (buffered)	5% titanium dioxide	60·5	65·7	96·0
Ammoniated mercury ointment	2·5% ammoniated mercury	68·5	73·5	96·3
Ammoniated mercury and coal tar ointment	2·5% ammoniated mercury	72·0	74·5	98·5

content, and particularly with the atomic number of the metals present. All the bases of the local applications have low mass absorption coefficients approximating to that of water. The addition of quite small percentages of metals of high atomic number to these bases results in mixtures with a much higher mass absorption coefficient.

(It may be noted that with the 90 kV x-radiation Compton scatter also is important as a method of absorption of the beam).

One of the authors (A. V. S.) calculated the theoretical absorption of x-rays by three of the local applications used, treating the non-metallic bases as being equivalent to water, and his results conform approximately with the experimental results.

Conclusions.

When Grenz ray treatment is to be given all local applications must be removed if this therapy is to be efficient. The most practical method of doing this is by advising the nursing staff to refrain from carrying out dressings for twelve hours prior to the treatment and if necessary by removing old applications with liquid paraffin. Last minute removal of ointments is to be deprecated as it tends to allow unnessary trauma to the affected skin. The same general rule applies to low voltage x-ray therapy, though here, if the local application absorbs a minimal percentage of the primary beam, this would not be absolutely necessary.

Summary.

(1) The absorption of Grenz rays and low voltage x-rays by 10 local applications was found by a simple experimental method.

(2) Results showed that the absorption varied with the metallic content of the preparations used.

We wish to thank Dr. W. A. Jennings, M.Sc., Ph.D., Physicist to the Royal Northern Hospital, for taking the readings with the Siemens dosage rate meter.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. G. B. Dowling.

21 May 1953.

Case for Diagnosis : Unilateral Orbital Pigmentation.—Dr. Henry Semon.

The patient aged 45 was first seen in January 1953. when he presented the clinical picture now apparent.

History.—On 6 February 1950 both antra were punctured and washed out under general anaesthesia for a suspected infection that might have a bearing on his asthmatic symptoms and a dubious report of " recent lung haemorrhages." The surgeon writes that at the operation 2 c.c. of a 5% argyrol solution were left in both antra as a precautionary measure, although the saline washouts had been returned clear.

There were no operative difficulties and no bleeding subsequently.

Between 5 and 6 a.m. next day he developed a " first class black eye with gross swelling of both upper and lower lids . . . and it was obvious that he had a large orbital haemorrhage." He was retained in hospital, and 2 weeks later some persistent pigmentation of the right orbital integument was noted, which it was thought would disappear in time. Six months later it was still present and has not, according to the patient, varied either in localization or intensity for nearly $3\frac{1}{2}$ years.

Histology.—Sections " are negative for silver deposits, but strongly positive for melanin granules (Fontana staining) in the lower layers of the Malpighian body."

Clinically this is an example of argyria but I was put off the diagnosis because the pathologist's report was negative for silver. Since then they have produced the granules which you have seen under the microscope. The history is very clear—the surgeon must have punctured the orbital plate of the antrum and introduced a small quantity of silver into the orbital tissues. The surgeon is emphatic that there was no haematoma until 5 o'clock the following morning.

I brought the case for an opinion as to whether any treatment is of the slightest use. In the literature there is a suggestion by two American dermatologists (Stillians and Lawless, *J. Amer. med. Assoc.*, 1929, **92**, 20) that these granules can be dissolved with 1% solution of potassium ferro-cyanide in 6% sodium thiosulphate. The injection is said to be intensely painful, and the results are not satisfactory because irregular pigmentation may supervene, so I have advised the patient not to submit to any surgical or injection treatment.

Dr. L. Forman : Is the discoloration due to silver or due to increase in melanin deposition? If the latter, as I suspect, it might be worth trying the effect of hydroquinones. Whether it would be worth doing or whether the silver would still be present—and I surmise it would be —I do not know.

Dr. Haber : The histology shows a hyperpigmented basal cell layer. The pigment is clearly seen to be disposed both through the epidermis by the normal course of keratinization, and pigmentary incontinence. One can therefore see pigment granules right up in the stratum corneum and widely spread within the corium. I think this is melanin. One cannot, of course, exclude a few granules of silver, but silver accumulates around epithelium of the sweat apparatus, and would not appear, and still be present, in the stratum basale after such a long time.

Dr. Alice Carleton : One can tattoo with different pigments to break up the lesion.

Dr. J. E. M. Wigley : I suggest that this is a minor disability, and instead of submitting the patient to a lot of procedures I think the old advice of " put a little powder on it " would meet the situation.

Dr. Bettley : The presence of silver in the skin may promote melanogenesis and stimulate the skin to produce pigmentation of the normal kind.

Dr. P. A. J. Smith : Is there any histological evidence that the patient has argyria? I looked at the slide and saw what Dr. Haber described. Is that the appearance of argyria or should we see silver in the dermis?

Dr. Semon : Dr. Beck of the Paddington Group Laboratories informs me that the pigment granules are bleached by the peroxide method, confirming his view that they are melanin deposits.

Multiple Epitheliomatosis.—Dr. S. P. Hall-Smith.

Miss L. H.—, aged 59

History.—For the past 20 years gradual development of flat, scaly and, more recently, crusted lesions on her chest, abdomen and back. She was first referred to hospital on this account 3 weeks ago.

She states that when aged 26 she developed epilepsy, though there have been no severe attacks for the past 10 years. Her doctor looked up her old notes and found that in 1923 one of his predecessors had put her on a mixture containing liquor arsenicalis—she took the equivalent of 3 minims three times a day for probably 4 or 5 years. As far as she knows she has taken no arsenical mixture since.

On examination.—Scattered superficial plaques, mostly of dry eczematous appearance with barely discernible rolled edge, involving anterior and posterior surfaces of trunk. The lesions vary from $\frac{1}{2}$ to 3 in. in diameter. Two lesions, one over the left chest and the other in the right iliac fossa, are ulcerated and crusted.

Histology (Dr. H. Haber).—Biopsy from eczematous-type lesion—superficial basal cell epithelioma.

Biopsy from ulcerated lesion—basal cell epithelioma.

Comment.—This patient is shown because of the history of arsenical medication over a prolonged period and the two clinical types of lesion. In view of the reports of Prosser Thomas (1939), Lomholt (1936) and Witten and Lazar (1952), I am tempted to treat the more superficial lesions with thorium X, but I should welcome the opinion of the section on the treatment of the ulcerated lesions.

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Dr. W. J. O'Donovan : My attention was first directed to the carcinogenic possibilities of arsenic after reading a paper by Pye-Smith (1913, *Lancet*, ii, 210 and 282) ; 28 cases were quoted and in nearly all the arsenic was taken medicinally. The other 2 were employed in the sheep dipping industry of which I was able to publish 6, 3 from Dr. Legge, similar cases in the *Brit. J. Derm.* (1924) **36**, 477. Arsenic cancer was certainly recognized by John Ayrton, in Paris (*Pharmacologia*, 4th ed. 1820, pp. 282). His beautifully written communication has been severely attacked recently, but it is difficult for a mind living in this century to pass a final criticism on records made a century ago.

This case affords me an opportunity to comment on the absence from our hospitals of any laboratory aid for the detection of arsenic. Purity of apparatus, air and re-agents is of supreme importance and were there a forensic room in our clinical laboratories the arsenical factor in many obscure eruptions would be, I am sure, revealed.

My most peculiar case of this nature was a research chemist with small palmar "warts" whose laboratory research life had been devoted for years to arsenical preparations. Dr. Hamilton (*Brit. J. Derm.* 1922, **34**, 15), recorded a case where arsenic had been taken for 36 years so that I would be hesitant to press the arsenical diagnosis of this interesting case as 3 years is a short period of administration unless the case shows also multiple arsenical keratoses.

I am cautious of a positive diagnosis that might lead to legal actions. I have this year dealt with the papers of 3 cases in which the patient and his advisers thought administration of arsenic inadvisable and negligent. One of these patients had taken arsenic for 20 years with unmistakable benefit for psoriasis. Erasmus Wilson used arsenic very freely and remote risks must properly be taken in the patients' interest.

For treatment I would advise half strength radium plates to be applied superficially three times in all with an interval between each treatment of at least 6 weeks.

Dr. R. T. Brain : Sequeira collected an impressive series of multiple epitheliomata of the skin that appeared to be sequelae to arsenic medication. I thought he was convinced of the significance of the association, although the incidence must be rare considering the popularity of the remedy in those days. I prefer excision when the lesion is suitable and there is plenty of redundant skin. CO_2 I would suggest should be used for at least 3 minutes, since recurrences follow inadequate freezing.

I am chary of thorium X for I have had cases sent to me that have failed to respond. There is no rational explanation of its efficacy at all considering that the mass of its energy is in the alpha rays which are stopped by tissue paper. These lesions must be extraordinarily superficial if they are cured with α or Grenz rays. My colleagues who use the fractional X-ray technique seem to deal with them effectively.

Dr. Andrew J. Hakendorf : I have seen a good deal of treatment of malignant growths of the skin with radiotherapy in Australia. I believe the small lesions in this patient would do very well with X-ray therapy.

The areas of involvement measuring approximately three centimetres in diameter would get an excellent cosmetic result with a total dose of 4,500 r, with a treatment of 500 r at each session ; the overall time should be about three weeks.

Dr. Bettley : I am very interested in the remarks about the absorption of the α particles. Professor Roberts looked at some thorium X that we were using in the clinic and found that there was also a very reasonable amount of β radiation as well. Dr. H. T. H. Wilson and I then painted the thorium X on to ourselves, using a layer of cellulose as a screen, which Professor Roberts assured us would stop alpha particles and any atoms or molecules penetrating ; it would not, of course, stop β or γ radiation. We found that we got not as much, but almost as much erythema by painting on screened thorium X as we got from unscreened application so that there is no doubt that much of the biological action of thorium X on the skin is due to the beta rays. There is also a certain amount of gamma rays.

I have treated one or two of these epitheliomas with thorium X. I think it does excellently. They need about 12 successive paintings, perhaps at intervals of a fortnight. We have used 1500 units per c.c. and each treatment has consisted of about 3 paintings repeated in succession as soon as it is dry. It works extremely well and produces the minimum scarring. It seems to be the treatment of choice.

Dr. Hall-Smith : I am most grateful for the many observations and views which have been given. It would be interesting to try Grenz rays on some of the lesions and thorium X on the others. I intended to use thorium X because the hospital where I saw this patient has no radiotherapy department, and thorium X is less painful than CO_2 snow. The ulcerated lesions will be excised.

Ichthyosis Vulgaris with Hyperkeratosis. –Dr. R. H. Marten for Dr. F. Ray Bettley.

H. K.—, aged 60.

Occupation.—Labourer.

History.—Has always had a dry skin, which does not improve in the warm weather, although he sweats normally in the summer.

There has never been any erythema, bullae or itching. For the past 30 years he has noticed warty lesions on the feet, knees and buttocks. These are painful at times and tend to bleed when removed. They have remained unchanged for many years and are not increasing in number.

Past history.—Has lived alone for 20 years. Probably eats an inadequate diet. No history of urethral discharge. Takes occasional tonics for lumbago and sciatica. No definite occupational contact with arsenic.

Family history.—Father had dry skin. Three children—skin normal.

Examination.—The skin is dry and scaly except for the flexures and folds where it is normal. Greyish, horny masses are present on the lower legs and dorsal and plantar aspects of the feet. The knees and lower part of the buttocks are affected to a lesser extent. Pitted and pigmented depressions are seen at the sites of former lesions. This is most marked over the lower legs and feet. The hands are unaffected and the scalp is normal. Toenails show marked onychogryphosis.

Investigations.—Hb. 108%. W.B.C. 15,000, normal differential. Platelets 180,000 per cm. Bleeding and clotting time normal. Hess test negative.

Blood W.R. and G.C.F.T. negative.

Urine—N.A.D.

Fasting blood sugar 102 mg. %.

Vitamin C saturation test normal.

Arsenic content of hair. 1·5 parts per million, consistent with mild chronic arsenical ingestion.

Histology.—Biopsy from left lower leg. Thinning of the epidermis with overlying hyperkeratosis, absent sebaceous glands and pigmentation in the dermis which proved to be haemosiderin.

Treatment.—Right leg only has been treated with a 10% salicylic acid ointment.

Discussion.

Cockayne listed a number of hyperkeratotic conditions affecting the feet, but I have been unable to find any record of a case exactly similar to the present one.

Investigations were normal, apart from the high arsenic content found in the hair and nails. There is no definite history of contact with or ingestion of arsenic, although the patient is not a very reliable witness.

The histology shows the changes of ichthyosis vulgaris and not those associated with arsenical keratosis or congenital ichthyosiform erythroderma. The absence of erythema and the sparing of the flexures are against this latter diagnosis.

The haemosiderin deposits in the dermis may perhaps be due to stasis. In the presence of an excessive amount of arsenic and hyperkeratosis it is difficult to avoid associating the two.

It may be that in this case arsenic has stimulated an ichthyotic skin to respond in this manner.

Reference.

Cockayne, E. A. (1933) *Inherited Abnormalities of the Skin and Appendages.* Oxford Medical Publications.

Dr. Theresa Kindler : A woman in the London Hospital who had had a dermatitis of her leg was advised by her doctor not to wash. She did not wash for a year and kept applying ointments. When we saw her first she showed a similar picture of thick keratotic crusts covering the lower half of one leg. The condition responded within a few months to potassium permanganate baths, eusol compresses, keratolytic applications and superficial x-ray treatment. I wonder if in the present patient the original ichthyotic tendency could have been increased by the stimulus of retention of secretion and the prolonged application of paraffin ointments.

Dr. Marten : This man has not a bath in his own house but assures me he goes to the public baths every fortnight.

Macular Atrophy with Syphilis.—Dr. I. S. Hodgson-Jones and Dr. C. S. Nicol.

J. T— aged 27. This typical " atrophic macular " rash has been present for 7 years.

It is not possible to say when he contracted syphilis, nor whether he actually had a secondary syphilitic eruption. He had a rash whilst in Singapore in 1946, which he says was " tropical rash " like the other troops had, and which was, perhaps, prickly heat rather than syphilis. Later he noticed the rash that he now has. The progress was insidious, but it was noticeable enough for him to report sick to his medical officer and to ask for a blood test, which was not carried out, however.

The patient has widespread macular atrophy and positive Wassermann and Kahn reactions. Histology shows almost complete loss of elastic fibres in the affected areas.

He is shown because this condition has always been rare and is likely to become even rarer in the future.

One of the problems that seems to be unanswered so far is whether these lesions can arise *de novo*, or whether they necessarily arise in an area of skin previously the site of a clinically apparent syphilitic lesion.

Dr. Nicol : I have little doubt that in 1947 this patient had secondary syphilis and I think that the macules have arisen at the site of the original papules. The first slide reminds you of the condition as we saw it to-day. The second comes from the collection of photographs in the department and shows a case of secondary syphilis with a rash of similar distribution. I show it in case anyone should think that the distribution in the patient we saw to-day did not occur in those with the rash of secondary syphilis. It may be said by some that macular atrophy is not connected with syphilis. This patient has syphilis and if we do not associate them in this case then we can never say that there is such an entity as syphilitic macular atrophy.

The President : All cases of syphilitic macular atrophy that have been published have been similar to the case we have seen to-day. I brought a patient here with identical lesions in 1927.* From the literature up to that time it was not clear whether the lesions were or were not usually preceded by a secondary eruption. Adamson quoted two in which an eruption had been present some 10 or 12 months before the macular atrophic lesions but he could not say whether atrophy had actually replaced the secondary lesions. My case had no recollection of having had a secondary eruption though he had gross tertiary syphilis when I saw him.

Dr. Bettley : I am not sure that I feel satisfied that this is macular atrophy. In macular atrophy the lesion should be sunken below the surface at least to the finger, whereas these lesions, some of them, are not only raised as you look at them, but there is an increase of substance there. If this is called atrophy it is a misnomer because there is something tumour-like about it. There is no history of syphilis here and no physical sign other than these very doubtful lesions. It is difficult to believe a man would get away with a florid eruption of secondary syphilis like this in the Royal Air Force in Singapore.

I believe this case belongs to the Schweninger-Buzzi group ; it is not sufficient to base a diagnosis of syphilis solely on the result of the W.R.

The President : That rather supports the view that syphilitic macular atrophy is not necessarily preceded by a secondary eruption.

Dr. Nicol : Sections of the skin lesions showed atrophy with destruction of the elastic tissue. About 60% of patients who report with latent syphilis have no memory whatsoever that they have passed through the primary or secondary stage of the disease. The fact that this patient asked for a blood test suggests that he was aware he had risked infection and as the medical officer did not agree with his request, it may well be that the diagnosis of secondary syphilis was missed at that time.

Dr. Hodgson-Jones : I must say that I think " atrophy " is rather a bad term; it is only a disappearance of the elastic tissues.

The following cases have been published in *Proc. R. Soc. Med.*, **46**, 906 :

Dermatofibrosarcoma Protuberans.—Dr. E. Waddington.
Epithelial Naevus.—Dr. R. J. Cairns.
Acute Lichen Planus Treated with A.C.T.H.—Dr. R. H. Meara (for Dr. G. B. Dowling).

The following cases also were shown :

Light Sensitive Epidermolysis Bullosa.—Dr. B. C. Tate.
Angioma Serpiginosum.—Dr. E. Lipman Cohen.
Favus, Mother and Child.—Dr. R. H. Meara (for Dr. G. B. Dowling).

* *Brit. J. Derm.* (1927), **39**, 55.

NORTH BRITISH DERMATOLOGICAL SOCIETY.

Glasgow, 8 October 1953.

Favus.—Dr. W. A. Dewar (for Dr. A. Girdwood Fergusson).

Case 1.—Mrs. F. W—, aged 39.

History.—The infection began on the scalp in childhood.

On examination (February 1951).—The scalp was erythematous with marked scaling and crusting. Areas of alopecia and a few favic scutula were present on the occipital region and over the central area of the scalp.

Case 2.—P. W—, aged 8, the daughter of Case 1.

History.—Lesions were first noticed on the scalp soon after birth.

On examination (February 1951).—The entire scalp was hyperaemic. Widespread alopecia was present and heavy crusting and favic scutula were very evident.

Investigations.—Wood's light examination revealed greyish-green fluorescing hairs in both cases. Microscopical examination showed hyphae and chains of large spores arranged in the long axes of the hairs. Air spaces were present. Cultures of hairs and crusts resulted in growth of *T. schoenleini.*

Treatment (March 1951).—X-ray epilation of scalp hair (414 r., 100 Kv., 1 mm. Al. filter, 5 field technique).

Progress.—A few grey-green fluorescing hairs became apparent in the hair regrowth five months after epilation in both patients, and on culture these resulted in growth of *T. schoenleini.* After three months of topical treatment with Decilderm ointment, Wood's light and cultural examination failed to reveal any indication of persisting infection. Regrowth of hair is now very satisfactory, with no evidence of infection. A few areas of alopecia remain over the parietal regions.

Congenital Bullous Ichthyosiform Erythroderma.—Dr. W. A. Dewar (for Dr. A. Girdwood Fergusson).

A woman aged 31.

This patient was shown to this Society when she was a child. At that time bullous lesions were present and the condition was more extensive. The face, trunk, limbs, hands and feet were all affected.

Present condition.—Greyish-brown thickened, warty plaques are present, especially in the axillary and inguinal regions and over the flexor aspects of the limbs. The skin of the trunk is markedly ichthyotic. The face, hands and feet appear normal. There is no erythroderma and there are no bullae.

Sarcoidosis (Darier-Roussy).—Dr. J. C. P. Logan (for Dr. A. Girdwood Fergusson).

A married woman, aged 47.

History. The patient complains of swellings of firm consistency on the right hand and forearm of eleven months' duration. They are neither painful nor tender.

Apart from anaemia during pregnancy twenty-three years ago there is no history of previous illness or skin disease.

On examination (3.iii.53).—On the dorsum of the right hand and forearm there are six lesions varying in size from a pea to a bean. They are subcutaneous and of firm consistency. The skin over the largest lesion on the dorsum of the right hand

is red-brown in colour, but the others are not pigmented. There is no lymphadenopathy.

The liver and spleen are not enlarged. B.P. 140/80.

Investigations.—Mantoux reaction, 1 : 10,000, negative ; serum calcium 10·1 mg.% ; blood cholesterol 166 mg.% ; blood urea 36 mg.% ; serum proteins 8·09 g.% (albumin 5·2, globulin 2·8).

Skiagrams : Hands and feet normal.

Chest : There are infiltrated changes in the lungs, more marked on the left side, consistent with sarcoidosis.

Histology (Dr. John A. Milne).—The epidermis is normal.

The corium is fibrosed and there are numerous sharply defined follicular aggregates of epithelioid cells and giant cells. These extend down into the subcutaneous fat. No foreign material is seen. The histological appearances are those of the sarcoid type of reaction.

Treatment and progress.—14.iii.53 : Calciferol (Ostelin), 50,000 units three times daily.

23.iv.53 : Lesions on right wrist seem unchanged but patient thinks they have improved.

18.vi.53 : Lesions appear to be resolving.

6.viii.53 : Lesions flatter. Treatment with calciferol discontinued.

27.viii.53 : Lesions regressing. Serum calcium and blood urea normal.

Parapsoriasis En Plaques (Brocq) Progressing to the Premycotic Stage of Mycosis Fungoides.—Dr. J. C. P. Logan (for Dr. A. Girdwood Fergusson).

A woman aged 64.

The patient was shown to this Society in October 1952. Since then, treatment with ultra-violet ray to individual lesions was continued at varying intervals until 3.iii.53. The lesions involuted temporarily with this treatment, the best results being obtained with 2nd and 3rd degree reactions.

In March 1953 a course of ACTH with given, 10 doses of 25 mg. 6-hourly followed by 30 doses of 10 mg. 6-hourly. The response was prompt, the plaques cleared and the patient remained well apart from slight sacral oedema. Maintenance with a dosage of 5 mg. daily was instituted, but the lesions recurred. Since April the patient has received no ACTH. Numerous patchy, erythemato-squamous lesions are present on the trunk, arms and thighs.

The following cases also were shown :

Dermatitis Artefacta.—Dr. W. Herbert Brown.

Urticaria Pigmentosa ; Epidermolysis Bullosa ; Angioma Cavernosum ; Multiple Idiopathic Hæmorrhagic Sarcoma. Dr. W. A. Dewar.

Lupus Erythematosus ; Mycosis Fungoides.—Dr. J. C. P. Logan.

Pemphigus Foliaceus ; Pemphigus Vegetans ; Benign Mucous Membrane Pemphigus ; Impetigo Contagiosa.—Dr. A. Girdwood Fergusson.

Leprosy.—Dr. J. C. P. Logan.

OBITUARY.

Professor B. DUJARDIN.

CAT.

His many friends in this country received with profound regret the news of the death of Professor Benoit Dujardin in Brussels on 1 December 1953.

Benoit Dujardin was born at Anderlecht in 1884. He graduated with distinction in medicine at the University of Brussels in 1908. He began his work in dermatology in the service of Professor A. Bayet at the Hôpital St. Pierre where he became a popular and effective teacher. In 1935 he was appointed head of the Department of Dermatology and Syphiligraphy of the University Hospitals and he became Professor Extraordinary in 1945.

During the Great War, after long service at the Front, he took charge of an Army Syphilis Unit at Havre and the experience he gained there increased his appreciation of the social importance of venereal disease. During the years after the War he devoted much time and energy to the problems of syphilis control. He was particularly interested in neurosyphilis, on which he became an acknowledged authority, and to our knowledge of which he made many important contributions. His monograph, *Le liquide cephalorachidien* (1921), is perhaps the best known. He achieved the distinction, rare indeed for a dermatologist, of election to the presidency of the Belgian Society of Neurology.

The list of his publications on dermatology and syphilology is an imposing one. In recent years he also contributed many scholarly and beautifully written articles on medical history ; he was interested especially in the history of syphilis and of scabies.

The many younger British dermatologists who knew Professor Dujardin after the Second World War will remember him best for the friendly welcome he always gave them, for his quiet and unassuming manner and for the unfailing charm and wide range of his conversation ; for he was a man of many interests, he loved music and the arts, and was a keen and discriminating collector.

Professor Dujardin was elected Honorary Foreign Member of the British Association of Dermatology in 1946.

A. J. R.

BOOK REVIEWS.

Proceedings of the Tenth International Congress of Dermatology.*

On all sides the Tenth International Congress of Dermatology was held to have been a great success and it is difficult to resist a comparison between this Congress and the somewhat sterile efforts of our political brethren and sisters. The success of the Congress has been worthily sustained and recorded in these Proceedings which might well serve as a model of their kind both in substance and presentation.

In the social report the first place must go to Dr. Dupont's admirable sketches of noted personalities of the Congress. To those who are fortunate enough to be familiar with Dr. Dupont's talents, the success of the sketches will come as no surprise and provide suitable leaven to the professional record. The panoramic photograph of members of the Congress also provides a most agreeable introduction, if necessarily somewhat more egalitarian than Dr. Dupont's sketches. In the photograph some very distinguished members of the Congress appear to be in various stages of eclipse.

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* Proceedings of the Tenth International Congress of Dermatology, London, 1952. (1953) London : British Medical Association. Pp. 556 + xxxix. Price £3 3*s*.

In the Proceedings of the Meetings it would be invidious and almost impossible to single out any sections for special praise. Perhaps the two sections which provoked most interest were the discussion on the use of cortisone and corticotropin and the record of the clinical meeting, even if the report of the former is likely to be of somewhat ephemeral value. The clinical meeting is particularly well reported, with excellent illustrations.

All members of the Congress will I am sure wish to congratulate the Editor and his colleagues on these wholly admirable Proceedings. H. J. W.

The T.P.I. Test.*

This book, consisting as it does of a series of studies, each the work of a different leading French syphilologist, demonstrates the early recognition by the French clinicians of the importance of the comparatively new Nelson-Mayer Test, or as it is more frequently called, the Treponema Pallidum Immobilization Test. Although a number of them prefer to remain sceptical of its ultimate value, no one denies its importance in the exposure of biological false positives, one of the remaining bugbears of the clinician faced with the treatment of a patient presenting a positive blood but neither history, signs, nor symptoms to account for it.

The present book surveys comprehensively every angle and aspect of the T.P.I. Test. It discusses in detail the techniques used in the laboratory, from the classical tests of Wassermann and Kahn up to the present day Nelson-Mayer Test. Their comparative value is assessed and their application to the treatment of the luetic patient is studied. Several chapters deal with the more recent American technical advances in carrying out the test; another chapter deals with the question of immunity in experimental syphilis, whose study is controlled and made more possible by the T.P.I.; a further chapter discusses the importance of the T.P.I. in diagnosis in tropical areas where leprosy, yaws and the rickettsias are endemic. Another chapter is devoted to the diagnostic and prognostic value of the test in the pregnant and in the newborn.

But the general opinion of the French clinicians seems to be guarded about the test's value in routine diagnosis, and they would seem to prefer to wait until more work has been done on it and until further information is available, before giving it equal place with the longer-standing and accepted diagnostic blood tests.

While the book is of undoubted value and interest to syphilologists and pathologists, particularly those engaged in serology, there is little in it of direct or immediate concern to the dermatologist. R. B.

Modern Trends—2nd Series.†

Let there be no confusion from the outset—this is not the First Series brought up to date, but a completely new book with a fresh team of 23 eminent contributors. As the editor points out, there is little connection between successive chapters but each is complete in itself, so that the pleasure of reading the book—and it is pleasure—can be prolonged.

In the first chapter on Ecology in Relation to Dermatology, Professor Leslie Banks paints in the background against which we see modern dermatology and even ventures to foresee into the future. Then follows a most painstaking analysis of the psychosomatic aspects of dermatology by Dr. Macalpine in which she shows how

*_The T.P.I. Test of Nelson-Mayer_. By J. Charpy. 1953. Paris: Masson et Cie. Pp. 348. Illus. 102. Price 2,500 fr.

†_Modern Trends in Dermatology_ (2nd Series). By R. M. B. MacKenna. London: Butterworth & Co. Ltd., 1953. Pp. 327. Figs. 58. Price 63_s_.

fully she understands dermatologists as well as skin patients. It is of interest that she believes, contrary to the opinion of most of the medical profession, that the emotional strain to which the dermatologist is exposed appears to be greater than in many other branches of medicine—even including psychiatry. Having been persuaded of the soundness of her ideas, I was all the more disappointed to find that her investigations into the cause of pruritus ani have led her to think that many cases are due to the reactivation of infantile unconscious fantasies centring on procreation taking place in the abdomen or intestines.

One is brought back to earth by the contributions on the anatomy, physiology and functional pathology of the skin which bring us up to date in the progress of these basic sciences. Other chapters deal with the present state of knowledge of the L.E. tests and the value of cytodiagnosis. Our American colleagues, Pillsbury and Kligman, add many interesting and hitherto unpublished facts on the bacteriology and disinfection of the skin ; their general rules for the clinical application of these findings are worthy of the widest circulation among all who deal with wounds and skin lesions, as is also the sound advice on the use of antibiotics given by Shooter.

There are also included chapters on the more chronic dermatoses due to tuberculosis, sarcoidosis and leprosy.

The cross-sensitization phenomena are dealt with in a most lucid way and Baer includes, most happily for those like the reviewer whose knowledge of organic chemistry is minimal, a child's guide to the aromatic compounds. Sulzberger, in a cautious and critical review of the results of treatment by ACTH and cortisone, adopts an optimistic view of the possibilities of the local use of hydrocortisone and gives to the clinician a hope for the future.

This underlines the whole atmosphere of the book, which is one of exciting progress. The editor and publishers are to be congratulated as keeping up the very high standard set by the First Series.

I. B. S.

CORRESPONDENCE.

To the Editor of ' The British Journal of Dermatology.'

Sir,—I read with interest the article by Dr. F. F. Hellier on anomalous histological findings in pemphigus which appears in the current issue of the Journal (p. 49).

I have under observation at present two cases which illustrate the problems in diagnosis encountered by us all in this fascinating field. Both present clinical features of so-called senile pemphigoid or benign pemphigus ; both can be extremely well controlled with ACTH but by no other drugs. In one biopsies have consistently shown sub-epidermal bullae, while in the other the clefts are intra-epidermal.

It has always been my view that the observations with regard to bleb formation in the bullous group of diseases expressed by Percival and Hannay (*Brit. J. Derm.*, 1949, **61**, 41, 77) may have been too cursorily brushed aside, and that the Tzanck method of differential diagnosis is perhaps too susceptible of erroneous interpretation.

I should like, therefore, to record my agreement with Hellier's suggestion as to the occasional (and perhaps more than occasional?) sub-epidermal position of the clefts in true pemphigus. It appears to me, moreover, that in the present state of our knowledge our diagnostic and prognostic pronouncements in cases of bullous diseases should continue to be based upon the clinical picture and response to treatment rather than upon histology.

I am, Yours, etc.,
A. Girdwood Fergusson.

3, Ashton Road, Glasgow, W.2 ;
20 February 1954.

CURRENT LITERATURE.

RESISTANCE OF PATHOGENIC BACTERIA. P. Hofmann. (1953) *Derm. Wschr.*, **127**, 275.

In the course of this discussion the author points out that antibiotics may have not only an inhibiting or indifferent action on bacteria but even on occasion in certain dilutions a stimulating one. He demonstrates this. With a dilution of 1 : 100 of a bacteriostatic the growth of typhus colonies on agar was inhibited ; but with a dilution of 1 : 100,000 the number exceeded by 176% that of a control without antibiotic or with antibiotic in a dilution of 1 : 50,000. With a dilution of 1 : 5,000,000 the effect became indifferent for the first time.

Not only bacterial sensitivity but an active body defence mechanism is essential for a favourable response to antibiotics. Certain antibiotics can replace immune bodies, e.g., the non-specific opsonin or the specific bacteriotropin important for phagocytosis. The author demonstrates this, using for his tests leucocytes, unencapsulated *Sarcina tetragena*, active guinea-pig serum (opsonin), normal saline alone, or containing 0·1% soluble prontosil, noting the percentage phagocytosis by the leucocytes after 5, 30 and 60 minutes with the various tests. Phagocytosis was highest with guinea-pig serum (opsonin) ; but little inferior by the end of an hour with normal saline containing 0·1% soluble prontosil instead of opsonin. Opsonin and prontosil together produced no better result than opsonin alone. Normal saline alone, without opsonin or prontosil, gave only a slight response. M. S. S.

ACRODERMATITIS CONTINUA HALLOPEAU. R. Frühwald. (1953) *Derm. Wschr.*, **127**, 269.

In a patient under the author's observation for 24 years the disease remained localized to one finger, then hand for 5 years : cleared temporarily with the appearance of widespread patches, to relapse rapidly when these subsided ; this continued for several years (attacks were pyrexial), then the hand healed with atrophy and contracture ; the disseminate eruption later became fixed and the limbs atrophied with contracture of large joints. M. S. S.

CHROMOBLASTOMYCOSIS IN QUEENSLAND. B. B. Barrack. (1952) *Austral. J. Derm.*, **1**, 207.

The disease is not uncommon in Queensland. It presents as painless warty cutaneous granulomata with spreading margins and little tendency to ulceration. It differs clinically from blastomycosis in that it runs a much slower course and dissemination is apparently unknown.

Diagnosis is confirmed by microscopy and culture. Differentiation from true blastomycosis, which has not yet been reported in Australia, is comparatively simple. The paper gives histological descriptions and discusses the mycology, remarking on the confusion existing in the classification of these fungi which are varieties of Fonsecaea, growing on Sabouraud's glucose agar.

Treatment is said to curb, but not necessarily to cure. Local fungicides and x-rays (2 4000 r in single or divided doses) are used. Potassium iodide in heavy dosage is continued for some months after apparent cure. R. B.

A SURVEY OF CHROMOBLASTOMYCOSIS IN QUEENSLAND. R. E. Powell. (1952) *Austral. J. Derm.*, **1**, 214.

35 proven cases in adult males were investigated (no female or child case recorded). The main facts elicited are as follows :

1. It is a disease of rural manual labourers.
2. The initial lesion was most frequently on exposed parts, and followed trauma in 12 cases.
3. It has not been possible to discover the alternative habitat of the organism.

This paper provides pictures of lesions, and a full and clear discussion of the mycology.

Treatment.—The author says it has been the practice at the Queensland Radium Institute to use a radon mould delivering approximately 4000 r over 7 days, and that the lesions respond well.

Twelve references are quoted in these two papers. R. B.

ANGIOMATA AND THEIR TREATMENT. F. C. Florance. **TREATMENT OF PROBLEM CASES OF ANGIOMATA OF INFANTS.** R. Kaye Scott. (1952) *Austral. J. Derm.*, **1**, 223 and 228.

It is generally accepted that—

1. Cavernous haemangiomata can resolve spontaneously.

2. Their disappearance seems to be hastened and sometimes initiated by exposure to some form of irradiation, or by other local therapy.

3. Portwine stains are very difficult to treat.

Dermatologists can be divided into—

(*a*) Those who believe that event (1) is so common that cavernous naevi should only be treated on certain definite indications : these usually include threats to the integrity of the eye or to the shape of the jaws. Members of group (*a*) are uneasy about the remote effects of radiotherapy, and include among them a number of crypto-herbalists.

(*b*) Similar to (*a*) but tending to give treatment where they consider that the parents' psychology demands it, especially if the lesion is on exposed parts.

(*c*) Those who treat all or nearly all lesions, believing that spontaneous resolution is uncommon. A subsection of group (*c*) is euphoric when considering x-ray sequelae.

Dr. Florance can be placed in group (*b*) ; Dr. Scott is a radiotherapist in group (*c*), but avoids being placed in the subsection. He is cautious when working near the eye, growing epiphyses, teeth and testes.

Some would consider it wise to extend this caution to the rudimentary breast, the thyroid, parathyroid, ovaries, and even the adrenal gland, all of which are surprisingly near to the surface in an infant. R. B.

THE PHYSICAL ASPECTS OF RADIATION TREATMENT OF ANGIOMATA. C. E. Eddy. (1952) *Austral. J. Derm.*, **1**, 234.

This is a good paper, listing not only the methods and effects of treatment on the lesions, but also the possible undesirable sequelae. The importance of considering the effects of x-ray on the deeper tissues is emphasized, and there is a valuable summary of the different methods by which these effects can be minimized. It is salutary to hear that there is not yet any precise information concerning the minimum dosage which can affect growing bones ; evidence is quoted to show that appreciable damage to bone growth in small animals can occur from epiphyseal (not skin) doses of little more than 500 r.

The possibility that x-rays may induce neoplastic change in later life is not considered in this article. R. B.

THE TREATMENT OF MICROSPORUM CANIS INFECTION OF THE SCALP WITH DIBROMOPROPAMIDINE ISETHIONATE. Miles Havyatt. (1952) *Austral. J. Derm.*, **1**, 239.

Twenty-five cases of *M. canis* ringworm treated with dibromopropamidine isethionate are compared with eleven cases treated with cupra-ammonium hydroxide.

Taking into account the varying degrees of inflammation before treatment was instituted, there was no significant difference between the results of the two groups. R. B.

RADIOTHERAPY EQUIPMENT OF USE IN DERMATOLOGY. C. E. Eddy. (1952) *Austral. J. Derm.*, **1**, 242.

This is a concise article written mainly from the point of view of a physicist. The requirements are clearly defined, and the various methods and machines are considered in relation to those needs. The output-characteristics of the usual superficial and Grenz tubes are given ; these are followed by sections on radium and radon and on the present and future place of radioactive isotopes. There is an astonishing amount of information in six pages (thirteen references). R. B.

FISTULA AURIS CONGENITA. G. F. Donald. (1952) *Austral. J. Derm.*, **1**, 253.

The condition occurs as a pit or sinus arising from the region of the first branchial cleft and appearing on or in front of the crus helicis, sometimes in adjacent areas. It may appear as a pinhead-sized pit, or as a sinus up to 15 mm. in length. It often discharges a white milky material, and may become infected or form a cyst or abscess.

This article reports seven males bilaterally affected in three generations of the same family. R. B.

CEMENT WORKERS' DERMATITIS. L. P. de Carvalho and E. B. Negreiros. (1952) *O Hospital*, **41**, 495.

The author patch-tested 30 workers in cement suffering from a vesicular dermatitis with 0·5% solution of potassium dichromate, to which 29 reacted positively. Only 3 reacted to lime. They conclude that this industrial disease is a manifestation of supersensitiveness to potassium dichromate that in no way depends on the age of the patient or how long he has been working in cement. G. W. B.

B.C.G. TREATMENT OF LUPUS ERYTHEMATOSUS. L. Baptista and N. Belliboni. (1952) *O Hospital*, **41**, 503.

A woman aged 52 with the symmetrical fixed type of eruption on the face which was slowly progressing despite treatment reacted positively to a Mantoux 1/1000 test, so attempts were made to desensitize her with oral B.C.G. 0·2 g. given weekly. After 3 doses the patches were less itchy and scaly, after 6 doses there was considerable improvement, and they had almost completely cleared after 9 doses. G. W. B.

HERPES GESTATIONIS. E. Klapötke and H. Langhof. (1953) *Derm. Wschr.*, **127**, 241.

This patient, with a history of recurrent herpes labialis, developed herpes gestationis during her fourth pregnancy. Inoculation of serum from a bulla (Berkefeld filtrate) on the cornea of a dog gave rise to a herpes-like eruption which could be transferred to a second dog in milder degree. Intracerebral inoculation gave no symptoms suggesting encephalitis. M. S. S.

BÜRGER-WINIGARTEN DISEASE. O. Saipt. (1953) *Derm. Wschr.*, **127**, 244.

Ulceration of one or both legs but freedom of the toes in 3 patients described : in 2 obliteration of the arterior tibial artery but collateral circulation through the posterior tibial. M. S. S.

EXPERIMENTAL INVESTIGATIONS ON THE NEOTEBEN TREATMENT OF TUBERCULOSIS. G. Veltman. (1953) *Derm. Wschr.*, **127**, 385.

Intraperitoneal inoculations of 185 guinea-pigs were made with neoteben-sensitive tubercle bacilli. The dosage varied from 10, 20 to 40 mg. per kg. of body weight and the onset of treatment from one day to 1, 2, 3 and 4 weeks after the inoculation. A further series received 10 mg. per kg. and a second 20 mg. orally. The untreated animals began to fail in 2–3 weeks and the treated ones gained weight. Even when treatment was begun 3–4 weeks after the infection nearly all could be saved from fatal miliary tuberculosis, but one or two died of generalized tuberculosis a few days after treatment begun 2–3 weeks after infection. Of 98 killed animals in whom investigations are complete, in 20, after neoteben treatment, and spite of further investigations and inoculations, there has been no evidence of tuberculosis. In 28, despite a good gain in weight, tubercle bacilli could be detected in organs or glands directly or by inoculation into guinea-pigs, neither the height of the dosage or duration of treatment showing a definite influence. After 100 injections 21 animals and after 200, 12 animals are all living in spite of cessation of treatment for 5 months. One only died a month after cessation of treatment with 118 injections of 20 mg. per kg., another 5 months after the end of treatment with 106 injections of 10 mg. per kg. Thus the prognosis for those still living is very uncertain. M. S. S.

EPICUTANEOUS AND MUCOUS MEMBRANE TESTS. F. Jakobs. (1953) *Derm. Wschr.*, **127**, 446.

The author considers that it is possible to distinguish an allergic reaction to a patch test from a toxic one ; an allergic one may extend beyond the confines of the patch and should itch ; a toxic one should be limited to the area of the patch and be accompanied by burning. Both types may exist together as with dapolin, the turpentine subsitute used in his experiments. Of 50 non-allergic subjects tested with neat solution 29 had a toxic reaction, and 1, such a reaction to 30%. He considers it necessary in some patients to increase the strength of the test solution beyond the minimum facultatively toxic concentration, e.g., to 70%, as in a patient he describes who only with that concentration was proved to be sensitive to floor polish (it is not made clear whether this was an allergic, toxic, or mixed type of reaction). In another patient using 80% it was of the mixed type.

In allergic reactions of the mucous membranes which may be accompanied by intractable dermatitis of the whole face and beyond, he advises testing both skin and mucous membrane as

one or other may not react. Among the methods suggested for the mucous membrane he suggests softening a plastic mould in hot water and fitting it to a space on the lower gum with a lamella for example of suspected dental plate or filling amalgam underneath—a freshly prepared and an old piece should be tested and left undisturbed for 8–10 hours. If mercury sensitivity is suspected merely painting with mercurochrome may suffice. M. S. S.

THE TESTING OF FUNGICIDAL AGENTS. A. M. Memmesheimer and H. Kuhlmann. (1953) *Derm. Wschr.*, **127**, 459.

The authors use the hanging drop method in testing various fungicides and describe the technique in detail. They find that microculture is in no way inferior to macroculture ; results are quicker and one can observe the type of growth. With all dilutions of asterol, for example, one can see changes in some of the spores in 24 hours, germination 24 hours later, and on the third day definite growth of hyphae. By this time the control culture shows vigorous growth and goes on to spore formation. The test culture on the other hand grows no further, but on transferring to asterol-free medium it grows again, normally indicating that asterol has a paralysing effect on hyphae but not on spores, permitting these to germinate. M. S. S.

MULTIPLE PROGRESSIVE ANGIOMATA (DARIER). O. Braun-Falco. (1953) *Derm. Wschr.*, **127**, 321.

In this girl aged 24 cavernous angiomata (11) had been appearing for almost two years. They were unusual in involving the trunk (shoulder and pelvic girdle) ; lesions present on right upper arm and back of hand, and red lip (like a melanoma) ; hazel nut to walnut in size many of grey blue colour ; hard elastic, or compressible, some tender on pressure and more uncomfortable just before or during menstruation. One recurred 6 months after excision. Histologically simple cavernous angiomata. One showed evidence of thrombosis whose obliteration and contracture indicates how they may disappear spontaneously. Negative family history and no history of haemorrhages. M. S. S.

DYSKERATOSIS. A. B. Hyman. (1953) *Dermatologica*, **106**, 101.

The term " dyskeratosis " has come to be used loosely and vaguely, and Hyman tries to give it more precise connotation. His conclusions are :

(1) Dyskeratosis is a particular morphological state of an individual cell, the result of faulty keratinization, appearing as a *corps rond* or a *grain*. Other cellular aberrations, without keratinization, are not to be designated " dyskeratotic."

(2) The only disease which shows both kinds of dyskeratotic cells to form a characteristic and predominant part of the picture is Darier's disease, which is, therefore, a dyskeratosis.

(3) The term " dyskeratosis " should not be applied to other clinical conditions where cellular dyskeratosis may be found, but is not an essential feature.

(4) The characteristic cells of molluscum contagiosum should not be referred to as dyskeratotic. The changes are not due to abnormal keratinization *per se*, but to virus inclusions.

(5) The Paget cell is not a dyskeratotic cell. The changes are not based on faulty keratinization in time or place.

(6) Bowen's disease usually contains dyskeratotic cells, but the diagnostic cells of Bowen's disease with clumped nuclei are not dyskeratotic, and the disorderly aggregate of cell types in this disease does not warrant the term " malignant dyskeratosis."

(7) The concept of accelerated and retarded dyskeratosis parallel with benignity and malignancy does not appear to be illuminating or tenable. J. F. S.

CORTISONE IN THE TREATMENT OF SYPHILITIC EYE DISEASE. A. N. Ashforth. (1953) *Brit. J. vener. Dis.*, **29**, 3.

In ocular inflammation of syphilitic origin the possible benefits of cortisone therapy must be set against the possible effects that systemic cortisone might have on the general syphilis. The author emphasizes that cortisone has not cured any condition in which it has been used. It is an adjuvant only to other general and local treatment, which must be actively applied. In syphilitic eye disease this concurrent treatment is possible, since the basic cause of the eye condition is known. Unfortunately in many other eye conditions treated this information is not so easily forthcoming. W. G. A.

PENICILLIN TREATMENT OF CARDIOVASCULAR SYPHILIS. Herman Beerman. (1953) *Brit. J. vener. Dis.*, **29**, 18.

A most comprehensive paper on this very important subject which it will repay all interested to read in detail. The author is convinced, as a result of his studies, that in penicillin practitioners have a safe, effective means of supplementing the medical treatment of cardiovascular syphilis. W. G. A.

FIXED ERUPTION DUE TO SULPHONAMIDE HYPERSENSITIVITY. Douglas J. Campbell and J. Oliver Doyle. (1953) *Brit. J. vener. Dis.*, **29**, 32.

Cutaneous reactions after using sulphonamide drugs are not uncommon. Fixed eruptions due to these drugs are comparatively rare. The authors describe two cases of "fixed drug eruption" due to sulphonamide hypersensitivity. In each case the characteristic feature was the recurrence of cutaneous lesions of identical nature and in identical sites after the administration of sulphonamide drugs. W. G. A.

TERRAMYCIN IN EARLY LYMPHOGRANULOMA VENEREUM. Keith S. Henley. (1953) *Brit. J. vener. Dis.*, **29**, 36.

Nineteen young adult West African males with early lymphogranuloma venereum were treated with terramycin 1 g. 6-hourly. Eighteen cases were cured in an average of just over 7 days. One patient failed to respond. The rate of cure is independent of co-existent latent syphilis. Terramycin is significantly more effective than the standard treatment with sulphonamides and antimony previously used. The literature on the treatment of lymphogranuloma venereum with the new antibiotics is briefly reviewed. W. G. A

EXPERIENCES WITH BAL. H. Langhof. (1953) *Derm. Wschr.*, **147**, 145.

Having noted the disappearance of arsenical keratoses and pigmentation with BAL the author tries it on other forms of keratoderma. Metals are stored in the sulphydryl containing basal layer of the epidermis, and the blocking action of the metal on this rich sulphydryl content allows hyperkeratosis and pigmentation to take place. In a patient with tylosis accompanied by leucokeratosis of the oral mucous membrane and severe lichen pilaris the mucous membrane lesions cleared, and the horny surface of the hands and feet became soft and could be scraped away: the inflammatory zone beyond the keratoderma was uninfluenced and the keratoderma returned on stopping BAL. In a man aged 60 with leucokeratosis of tongue and oral mucous membrane with diffuse keratosis of hands and feet and multiple warts on the trunk all lesions disappeared with injections of BAL and there was no recurrence when seen 6 months later. The garlic-like odour of BAL would be a disadvantage in its possible local use. In a patient with melanodermatitis toxica treated with BAL the pigmentation faded in about 8 days but the follicular hyperkeratosis only with additional local vitamin A treatment. Investigations showed an increase in serum histidine and phenylalanine and a very high tyrosine content. The sulphur-containing amino-acids cystine and methionine and the oxyamino-acids threonine and serine were reduced. Cystine was excreted abundantly in the urine. Values returned to normal on stopping BAL. Three patients with light sensitization eczema responded well to BAL. Light sensitization is said to depend on an oxydation of the tissues owing to the action of a sensitizer activated by light. The reducer BAL by combining with the peroxydase prevents the pathological reaction to light. M. S. S.

SPECULATIONS ON ECZEMATIDES IN SEBORRHOEICS. V. A. Puccinelli. (1952) *G. ital. Derm. Sif.*, **93**, 349.

The author traces the development of the conception of seborrhoeic eczema from that of Brocq and Unna, through the division between the German and French schools of thought, to the more recent Anglo-Saxon views. This difficult subject is well presented, though the author takes care to note that it is very difficult to define the exact limits of this group of diseases. It may be thought by some that the pityrosporum is given too prominent a place among the factors mentioned. The author attempts to correlate these as follows :—some metabolic disorder giving rise to an increase in the skin fats—a growth of the *Pityrosporum ovale* as a saprophyte—diminution of the cutaneous defences by the action of this organism, leading finally to the stage of secondary infection and histological spongiosis. D. S. W.

NODULAR DERMAL ALLERGIDES. H. Gougerot. (1951) *Minerva Medica*, **26**, 39.

"Trisymptome" and its variants are fully described. A lucid article which attempts to bring together a wide group of allergic reactions, ranging from thrombocytopenic purpura to papulonecrotic tuberculides and dermatitis nodularis necrotica. The author believes that the condition represents a dermal defence reaction against embolic attack from within. Well-documented references to all the varieties are given. D. S. W.

THE 17-KETOSTEROIDS IN SOME SKIN DISEASES. T. Taccialenza. (1950) *G. ital. Derm. Sif.*, **92**, 1.

By the method used the normal excretion was found to average 14·6 mg. per 24 hours in males and 11·2 mg. in females, though there were wide individual variations. In comparison with the 20 controls tested, a series of 16 female patients with acne had a raised value, and 23 patients with psoriasis a lowered value. Some figures are also given for other conditions. In scleroderma, for instance, the values appear to be lowered. D. S. W.

ANTIBIOTIC THERAPY IN SOME SKIN CONDITIONS OF UNKNOWN AETIOLOGY. T. Taccialenza and A. G. Bolloni. (1950) *G. ital. Derm. Sif.*, **91**, 418.

A useful and straightforward account of the treatment of cases of pemphigus, dermatitis herpetiformis, acrodermatitis of Hallopeau, dermatomyositis, scleroderma, herpes zoster, Weber-Christian disease, and others, in which various antibiotics have been given in considerable strength for varying lengths of time. The authors have found no evidence of cure in these diseases, and only in a few cases of pemphigus and dermatitis herpetiformis did there seem to be even a temporary amelioration. A very full bibliography is appended. D. S. W.

MORPHOLOGICAL CHANGES OF GUINEA-PIG SKIN ON INUNCTION. H. H. Berres. (1952) *Arch. Derm. Syph., Berl.*, **194**, 259.

Various ointments on one side, no ointments on the other; histological section showed that ointment bases tended to produce oedema and acanthosis. Least active were white paraffin and a silicon paste. M. F.

ANTIHYALURONIDASE EFFECT OF ANTIHISTAMINES. O. Braun-Falco and G. Weber. (1952) *Arch. Derm. Syph., Berl.*, **194**, 392.

The disappearance rate of intracutaneous wheals, increased by the addition of hyaluronidase, was inhibited partly by an antihistamine. However, the action of the antihistamine appears not so much to antagonise the enzyme as to affect capillary permeability—an indirect action. M. F.

STROPHULUS AND DIET. H. W. Siemens and A. A. Botter. (1952) *Arch. Derm. Syph., Berl.*, **194**, 84.

During 20 years papular urticaria could never be produced in children while in hospital by feeding the article of diet to which they were allegedly sensitive. In fact no evidence of an allergic origin could be found. Painting with tar prophylactically was no use—in contrast to allergic eczema, prurigo, psoriasis, etc. M. F.

THE PROBLEM OF CELLULAR NAEVI. C. Voss. (1952) *Arch. Derm. Syph., Berl.*, **194**, 30.

A pathologist reviews all the theories, stains his sections with silver and concludes: the cellular naevus is a complex neurogenic malformation, of neuroectodermal and neuromesodermal origin. Dendritic chromatophores and dendritic cells belong to the same system. Probably the cellular naevus is a hamartoma of the termination of a sensory nerve. M. F.

BALANITIS CIRCINATA IN REITER'S DISEASE. H. Reich. (1952) *Arch. Derm. Syph., Berl.*, **194**, 1.

It may be the only cutaneous manifestation of Reiter's disease and therefore serve for diagnosis. The histological description (with photomicrographs) is said to be the first recorded. The stratum corneum is parakeratotic and Reich likes the name balanitis circinata parakeratotica. A most impressive bibliography covers ten pages. M. F.